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IATROGENIC DISEASE AND ANAESTHESIA*

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Knowledge of the action of anaesthetic drugs has increased in recent years, and with the advent of muscle relaxants and new techniques there remain few absolute contraindications to the use of anaesthesia. Some techniques are known to produce adverse effects in certain pathological conditions, such as spinal analgesia in the presence of disease of the central nervous system or the use of thiopentone in porphyria. However, more recently it has become apparent that many forms of routine medical treatment may affect the response to anaesthesia. This paper deals with some of these, and a more descriptive title would have been "The immediate and remote adverse influences of some routine forms of medical treatment on the response of patients to drugs used in anaesthesia and their effect on the mortality associated with the deliberate production of unconsciousness." The title is intended to refer to maladies and abnormal states which are unwittingly produced by physicians, other than anaesthetists, and for which the anaesthetic technique may well be blamed.

Sulphonamides

These were probably the first drugs that were thought to influence the effects of anaesthetics. Because of their sulphur, it was suggested in the early 1940's that their use precluded the administration of thiobarbiturates such as thiopentone, in case sulphaemoglobinaemia might occur (Mallinson, 1941). They were said to intensify cyanosis and increase the toxicity of the thiobarbiturates, but this is no longer believed. Clinical experience has shown that thiopentone can safely be given to patients on sulphonamide therapy.

Hypotensive Drugs

Methonium Compounds.—In 1951 Davison warned anaesthetists to be aware of patients who were being treated with either pentamethonium or hexamethonium. At that time these compounds were being widely used as therapy for peptic ulceration, and should the ulcer perforate in such a patient he would be in a very grave pre-operative condition. The hypotensive effect of the methonium compound is more marked in the anaesthetized than in the conscious subject, and the hazard of anaesthesia in patients receiving these drugs is obvious. This is not merely a theoretical consideration, as the following reports will show.

Case 1.—Operation of transthoracic vagotomy on a patient who was on hexamethonium therapy. A severe fall in blood pressure occurred during induction of anaesthesia, and became more marked when the patient was placed in the lateral position and the bridge on the operating table raised. The hypotension responded to infusion of L-noradrenaline, and the operation was carried out after a delay of almost one hour.

Case 2.—Perforated peptic ulcer in a patient on methonium therapy. Sudden death followed induction of anaesthesia with thiopentone and a muscle relaxant.

Case 3.—Proposed thoraco-lumbar sympathectomy on a patient who was on pentolinium ("ansolysen") therapy. A severe fall in blood pressure followed induction of anaesthesia and was accentuated by posturing the patient on the table. There was not a good response to intravenous methylamphetamine, and the operation was abandoned. The patient was very clouded mentally for several days after this incident and the possibility of cerebral thrombosis was considered.

In none of these cases was the anaesthetist aware of the methonium therapy. Had this been known the operation should have been postponed in Cases 1 and 3, and the administration of phenylephrine, methoxamine, or L-noradrenaline might have prevented the fatal outcome in Case 2. As is shown below, with other drugs, many of the hazards described can be prevented by letting the anaesthetist know what medical treatment is being carried out, and by anaesthetists being aware that some forms of routine medical treatment can modify the response to anaesthesia.

Mecamylamine.—Recent work in cats by Payne (1957) has shown that, after its administration, hexamethonium and trimetaphan camphorsulphonate produced neuromuscular block. There is a potential risk if this is eventually shown to apply to man. It is to be expected that patients receiving this drug are liable to the same changes in blood pressure during anaesthesia as patients on hexamethonium.

Rauwolfia.—This is not a ganglion-blocking drug, but causes hypotension by central depression of the vasomotor system. The lassitude and drowsiness which it causes suggest that it may potentiate narcotics. Coakley and his colleagues (1956) studied the circulatory changes during anaesthesia in 40 cases receiving rauwolfia therapy. Of these, 40% had a fall in blood pressure of more than 40 mm. Hg and a pulse rate below 60 a minute. The hypotension responded in a variable manner to vasopressors, but relieving the bradycardia with atropine or oxyphenonium ("antrenyl") was of help. In addition to the above, rauwolfia potentiates ganglion-blocking drugs and produces nasal congestion and excess salivation. There may be difficulty in maintaining a clear airway, and the risk of excessive bleeding after nasal intubation is increased. Rauwolfia has a

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slow onset of action, and its effects last for several weeks. Where possible the drug should be stopped two weeks before operation.

Veratrum Alkaloids.—The effect of these alkaloids on the cardiovascular system is complex and incompletely understood. Their main action is a reflex fall in blood pressure and a reflex fall in pulse rate, known as the von Bezold effect (Dawes *et al.*, 1951). This can be very confusing when it occurs in the anaesthetized subject.

Case 4.—A married woman aged 40. Hypertension for many years. B.P. 195/100. Treated for two weeks with "rauwiloid" and "veriloid" tablets. Operation was craniotomy and ligation of aneurysm carried out under hypothermia. Fig. 1 shows the course of anaesthesia. Note

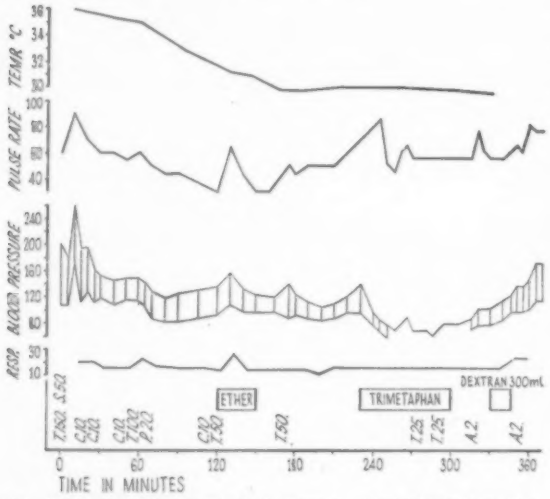

FIG. 1.—Course of anaesthesia in Case 4. T=Thiopentone. P=Pethidine. C=Chlorpromazine. A=Oxyphenonium.

initial tachycardia with ether, accompanied by rise in blood pressure and same effect with trimetaphan. The hypotensive action of the trimetaphan was rapidly reversed by two 2-mg. doses of oxyphenonium.

It can be seen that all drugs currently used in the treatment of hypertension can affect the course of anaesthesia. It is essential that the anaesthetist knows well in advance of the operation when such drugs are being given, and on occasion it may be advisable to postpone surgery until their effects have worn off.

Cortisone, its Analogues, and Corticotrophin

It has been known for many years that patients with adrenocortical insufficiency tolerate poorly the stress of anaesthesia and surgery. In 1931 Rowntree and Snell stated that the risk of any surgical procedure in patients with Addison's disease was prohibitive, but modern substitution therapy has completely changed the picture. A review of reported anaesthetics to patients with Addison's disease (Dundee, 1957) reveals that out of 18 cases with no special pre-operative preparation 89% developed hypotension during or after anaesthesia and the mortality was 56%. In comparison, hypotension occurred in only 55% of 20 patients who received specific hormone therapy and there was no mortality associated with the anaesthesia.

This applies to all types of adrenal failure, including secondary hypoadrenocorticism caused by inhibition of the pituitary by cortisone or corticotrophin. Welbourne (1957) has called this primary pituitary failure, which is a more descriptive term. Cortisone inhibits the pituitary directly. Corticotrophin stimulates the cortex to produce an excessive amount of cortisol, which in turn causes pituitary inhibition. After these substances have been withdrawn the pituitary–adrenal axis may take several months to recover normal function.

In adrenocortical insufficiency, patients react to the stress of anaesthesia and surgery by hypotension (out of proportion to the blood loss), respiratory depression, and delayed recovery. Different degrees of response are seen, depending on the severity of the condition and the stress. There are many published cases of peripheral circulatory failure developing during or after anaesthesia in patients who had cortisone therapy which was stopped within the three months before operation, or in patients in whom treatment was continued up to the day before operation, but where the all-important pre-operative dose was missed. One reported case got the pre-operative dose, but because of a delayed recovery from anaesthesia missed the evening dose and circulatory failure resulted. It is worth noting that in many incidences the operation was a minor one, not related to the condition for which the cortisone was given, and the period of anaesthesia was very brief. Procedures such as manipulation of a joint (Harnagel and Kramer, 1955), reduction of a dislocated shoulder, and dilatation and curettage (Dundee, 1957) have all been followed by profound hypotension in patients with primary pituitary failure.

Catastrophes from drug-induced adrenocortical failure are entirely preventable. In patients who are already receiving cortisone or corticotrophin an increased dosage should be given before operation. In patients who have stopped treatment within six months of surgery the problem is greater, especially in emergency cases, where it may not be known that such drugs had been used.

During the pre-operative examination all patients should be questioned regarding steroid therapy. One of the Chicago hospitals emphasizes the necessity for this, by having a special place on the anaesthetic record to note the pre-operative use of cortisone or corticotrophin (Karp, 1957). It must be remembered that prednisone and prednisolone are also powerful inhibitors of the pituitary, and their continued use may be followed by adrenocortical hypofunction. Surgeons will now feel happier about the cortisone therapy in view of the recent report by Popert and Davis (1958) that therapeutic doses do not interfere with wound healing.

There can be few better examples in medical practice of the saying "prevention is better than cure" than in the pre-operative management of adrenocortical insufficiency. This is illustrated by the following two cases.

Case 5.—A married woman aged 36 had a four-years history of diarrhoea. Motions varied significantly in frequency and con-

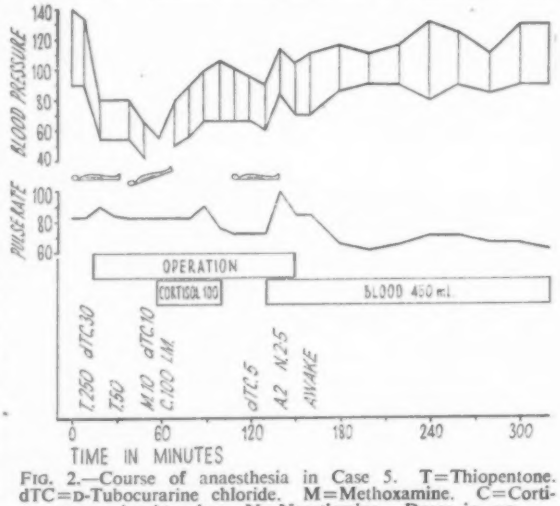

FIG. 2.—Course of anaesthesia in Case 5. T=Thiopentone. dTC=D-Tubocurarine chloride. M=Methoxamine. C=Cortisone. A=Atropine. N=Neostigmine. Doses in mg.

sistency with corticotrophin. General condition was good. Sigmoidoscopy showed purulent granular mucosa, but no ulceration. Barium enema showed whole colon to be spastic and devoid of haustrations ; the terminal ileum was also affected. Operation was colectomy and ileo-rectal anastomosis. Pre-operative steroid therapy: 16–15 months, 20–30 units of corticotrophin daily ; 14 months, 25 mg. of cortisone four times a day ; 13–9 months, 20–30 units of corticotrophin daily ; 8–3 months, 10–20 mg. of prednisolone daily; 2 months to 3 days, 20 units of corticotrophin daily. Pre-operative medication: promethazine, 25 mg., and atropine, 0.6 mg. Anaesthesia: thiopentone, D-tubocurarine, and N_2O–O_2 with mechanically controlled respiration. B.P. and pulse changes are shown in Fig. 2. The fall in blood pressure following induction was first attributed to the promethazine, and caused alarm only after it failed to respond to lowering the head of the table and intravenous methoxamine. Up to this stage the anaesthetist was not aware of the pre-operative steroid therapy. The response to cortisone and cortisol was dramatic, and thereafter the patient caused no further concern. Cortisone and corticotrophin were given in gradually decreasing doses for the first four to five days after operation.

Case 6.—A married woman aged 54 had had transverse colostomy performed for ulcerative colitis one year previously. At

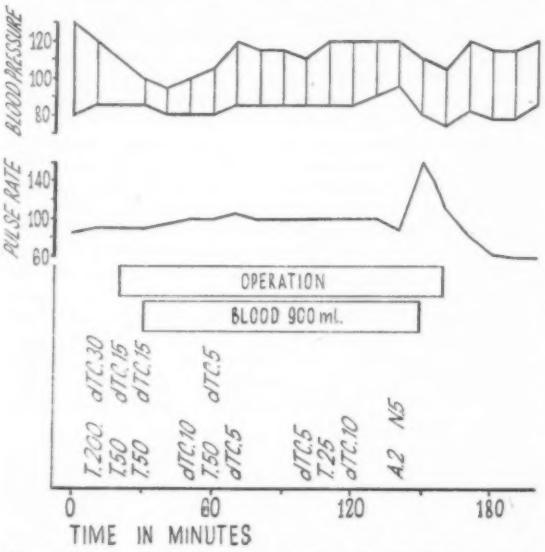

FIG. 3.—Course of anaesthesia in Case 6. T=Thiopentone. dTC=D-Tubocurarine chloride. A=Atropine. N=Neostigmine.

that time there was an ulcerating area round the anus with a stricture of the rectum. The anal conditions had improved, although there was still some blood-stained purulent discharge per rectum and bleeding from the mucosa of the colostomy. Weight 91 lb. (41 kg.). Operation: abdomino-perineal resection of rectum and colon and terminal ileostomy. Pre-operative medication: cortisone, 100 mg. ; corticotrophin 20 units ; pethidine, 50 mg.; atropine, 0.6 mg. Anaesthesia was with the same technique as in Case 5 and there was no severe fall in blood pressure (Fig. 3). The only notable feature was marked resistance to D-tubocurarine, which may have been due to the liver dysfunction which was present, with an associated low pseudocholinesterase level. The post-operative period, during which corticotrophin and cortisone were continued, was uneventful.

In these cases the most marked fall in blood pressure occurred in the patient who had the less extensive operation and who was thought to be in the better pre-operative condition. In cases of adrenocortical hypofunction, hypotension responds rapidly to intravenous cortisol, but the usual attention should be paid to blood replacement and avoidance of hypoxia and hypercarbia.

Tranquillizers

The intensity of the search for ataraxia is shown by a recent review article which estimates that 50 million pounds' worth of tranquillizers were sold in the United States in 1956 (Gold and Stone, 1957). From the point of view of modifying response to anaesthesia the phenothiazine derivatives are the most important group, and the effects of chlorpromazine have been studied in detail. Other members of this series vary in their action in degree only and possess, to a greater or less extent, the same hazards as chlorpromazine. They include such drugs as promazine (" sparine "), promethazine (" phenergan "), acetypromazine (" notensil "), pecazine (" pacatal "), and prochlorperazine (" stemetil ").

The effects of chlorpromazine vary with the duration of the treatment, dosage, route of administration, and the temporal relation of the last dose to the induction of anaesthesia. Long-term use continued up to the induction of anaesthesia can greatly prolong the duration of action of both narcotics and relaxants. Scanlon (1955) has described prolonged apnoea and delayed return of consciousness following thiopentone, gallamine, N_2O–O_2 and ether given for appendicectomy in a patient who had been receiving 25 mg. of chlorpromazine three times daily for 14 months. Even a single pre-operative dose of chlorpromazine can greatly reduce the dose of thiopentone needed to produce sleep, and if large doses of the thiobarbiturate are given there will be some delay in return of consciousness. Surprisingly enough, in animals the long-term use of chlorpromazine, if discontinued for at least 24 hours before anaesthesia, can cause resistance to the thiobarbiturates. This is seen clinically to some extent in patients who have had chlorpromazine for the treatment of subarachnoid haemorrhage or head injuries. Any of the above effects may be modified if liver function has been depressed by the long-term use of the phenothiazines.

More important than its action in potentiating narcotics and relaxants are the cardiovascular effects of chlorpromazine. The drug itself can cause hypotension and tachycardia, both of which are increased by the head-up tilt and in the presence of hypovolaemia. Like the methonium compounds, it potentiates the hypotensive action of thiopentone. Because of its adrenolytic action, one would expect a severe fall in blood pressure in patients who have received chlorpromazine before ether anaesthesia. (Price (1957) has demonstrated an increase in circulating adrenaline during ether anaesthesia, and Brewster *et al.* (1953) have attributed its stimulating action on the cardiovascular system to reflex release of adrenaline. The increased cardiac output caused by ether anaesthesia in normal dogs is replaced by a marked decrease if measures such as adrenalectomy and chemical blockade are taken to prevent the sympathetic discharge caused by the ether.) This effect is not of great clinical importance, but it must be remembered that after chlorpromazine much smaller doses of ether are required. If concentrations comparable to those used in patients who have not had chlorpromazine are given, then severe hypotension may result.

Tachyphylaxis to the hypotensive effects of chlorpromazine follows its prolonged use. This is important when the drug is used as an adjuvant in the production of hypothermia by surface cooling. It is frequently found that under these circmstances normal doses are quite ineffective in producing peripheral vasodilatation. The long-term use of chlorpromazine also seems to induce resistance to ganglion-blocking drugs.

Animal experiments have shown that chlorpromazine modifies the response to vasopressor drugs (Bourgeois-Gavardin *et al.*, 1955). The action of the less potent sympa-

Response to Vasopressors in Patients who Received Chlorpromazine

Drug	Dose	No. of Times Used	Good Response	Max. Rise of 20 mm. Systolic	No Response
L-noradrenaline ..		11	10 (91%)	1	0
Phenylephrine ..	2–10 mg.	10	9 (90%)	1	0
Methylamphetamine	8–60 mg.	9	1 (11%)	3	5
Methoxamine ..	5–20 mg.	13	3 (23%)	5	5

theticotonic drugs, such as ephedrine and methylamphetamine, is prevented completely, whereas the action of potent vasopressors is modified, but not inhibited completely, even by large doses of chlorpromazine. The importance of this in clinical practice is shown in the accompanying Table. The patients in this series all received at least 50 mg. of chlorpromazine before or during neurosurgical operations, and it can be seen that phenylephrine, in doses of 2–5 mg., is the most useful single-dose vasopressor under these circumstances.

Sedatives and Analgesics

The long-term use of these drugs is known to lead to tolerance to their desired therapeutic effects. This in turn causes cross-tolerance to the drugs used in anaesthesia. The intravenous thiobarbiturates are the best-known example, but this is probably because their actual dosage can be accurately measured and tolerance will be more easily detected. Increased dosage of curare-like relaxants is also required in patients who are tolerant to analgesics.

Unfortunately, resistance to thiopentone and similar drugs is more often seen in the type of patient to whom one does not wish to give large doses. It can be counteracted to some extent by increasing the pre-operative dose of morphine or pethidine, or by increasing the dose of relaxants used.

Another routine use of analgesics and sedatives which can cause trouble during anaesthesia is their subcutaneous administration to patients with peripheral circulatory failure. Because of their malabsorption more than one dose may be given, and when the vasodilatation due to the anaesthesia occurs or when adequate resuscitation has taken place these large doses will be released into the general circulation. There are many reported examples of respiratory depression at the end of operation which could be attributed to this cause. It is worth noting that both neostigmine and pyridostigmine can potentiate the effects of analgesics and possibly increase the degree of respiratory depression.

Drugs used in Treatment of Parkinsonism

It has been shown experimentally by Pulver (1955) that caramiphen ("parpanit," "panparnit") can potentiate barbiturates. There are no clinical reports of the significance of this action, and no explanation can be offered for the effect save that it may reduce muscle tone and that delayed recovery may be more apparent than real. However, a similar drug, benzhexol ("artane," "pipanol"), does seem to have some peculiar effect on the action of anaesthetics and possibly on muscle relaxants. Three cases of abnormal response to anaesthesia after its use have been brought to my attention, and the following report is typical of the sequence of events.

Case 7.—A 45-year-old man had been diagnosed as suffering from post-encephalitic Parkinsonism 19 years ago. For many years he had been treated with belladonna mixtures, but for the past four years had received benzhexol. The daily dosage at the time of operation was about 20 mg. Operation: orthopaedic emergency. Pre-operative medication: morphine, 10 mg., and atropine, 0.6 mg. Anaesthesia was induced with 350 mg. of 2.5% thiopentone and oral intubation carried out after 40 mg. of suxamethonium. As there was no return of spontaneous respiration the patient was inflated with nitrous oxide and oxygen and his general condition gave no cause for concern. He was still apnoeic 25 minutes later, when the operation was completed. After one hour he appeared to be remarkably light and objected to pulling on the tube, although he made no attempt to breathe. Extubation and reintubation was of no avail. In view of the muscle tone which was present it did not seem as if this was a case of suxamethonium apnoea, and bemegride was given without response. Nalorphine likewise produced no improvement. The eyelash reflex returned after 100 minutes and he was breathing periodically 50 minutes later. Three and a half hours later he opened his eyes when shouted at. His condition was not normal for a further two to three hours. He would sit up in bed suddenly and stare wildly, then lapse back again. The post-operative behaviour somewhat resembled the oculogyric crises of encephalitis lethargica or post-encephalitic tic.

One case of benzhexol-barbiturate poisoning showed no response to bemegride–amiphenazole and remained apnoeic for four hours and unconscious for three days. This is suggestive of some synergism between the barbiturates and anti-Parkinsonism drugs.

Ethopropazine hydrochloride ("lysivane"), a phenothiazine derivative, also used in the treatment of Parkinsonism, can be incriminated as a possible cause of prolonged apnoea and delayed recovery in another case. The potentiation in this patient may have been due to the same causes as those responsible for the prolongation of barbiturate narcosis by chlorpromazine (Dundee and Scott, 1958).

No explanation can at present be offered for the effect of anti-Parkinsonism drugs on the response to anaesthesia. It is not even certain whether the drugs themselves were to blame, and certain cases of Parkinsonism may themselves react abnormally to anaesthesia. However, this is unlikely, as there are no reported cases in the literature.

Oral Fluids

Out of 589 fatalities associated with anaesthesia, reported by Edwards *et al.* (1956), the largest single cause of death was regurgitation and vomiting followed by aspiration. Of the 110 deaths from this cause, 70% occurred in surgical emergencies, but two groups come within the scope of the present discussion.

Diabetics.—There were six deaths in cases where oral glucose solution was given pre-operatively, as is customary, and subsequent regurgitation or vomiting of fluid brought about the death of the patient. On five of these the operation to be performed was quite trivial. Water passes rapidly into the duodenum, but hypertonic glucose solution prolongs the emptying time of the stomach. In some animals the solution has to be diluted in the stomach until it is isotonic before it passes into the duodenum. Morton and Wylie (1951) suggest this as a possible explanation for these unfortunate occurrences. It is recommended that the practice of giving glucose solution by mouth be discontinued. If pre-operative glucose is essential it should always be given by the intravenous route.

Obstetrics.—Apart from the report already referred to, in which 15 deaths occurred from vomiting or regurgitation during delivery, there have been many publications drawing attention to this hazard, notably those of Parker (1954, 1956). The inhalation of liquid material can cause an asthmatic type of attack, with bronchospasm, pulmonary oedema, and cardiac failure. Death usually occurs within 36 hours of delivery. Much has been written about the prevention of these deaths during forceps delivery or caesarean section. The greater use of local analgesia, abandonment of the lithotomy position, and the routine passage of widebore stomach tubes before induction of anaesthesia have all been recommended. The answer probably lies in appreciating that absorption from the intestine is disturbed during parturition. Hawkins and Nixon (1957) have confirmed that this occurs during labour lasting more than a few hours. The *Lancet* (1957) admirably summarizes the situation: "There is little point in forcing solid food and extra fluids by mouth once labour has lasted more than 24 hours, for the material will often not be absorbed and merely encourage vomiting, thus increasing the risk of inhalation of stomach contents if anaesthesia has to be induced."

Radiation Therapy

Wilson (1955) found that animals exposed to *x*-ray therapy of the whole body showed an exceptionally poor tolerance to cyclopropane, but not to ether, ethylene, nitrous oxide, or thiopentone. Death resulted from respiratory failure occurring at an abnormally light plane of anaesthesia.

One reported case (Foster, 1956a) suggests that these findings may be applicable to man. Following deep *x*-ray therapy to a carcinoma of the mouth five weeks before operation, it proved impossible to maintain the patient on

cyclopropane because of the extreme and unusual sensitivity that he showed. A gas flow of 200 ml. a minute produced respiratory arrest for approximately half an hour, and the patient responded to painful stimuli before respirations became properly re-established.

Several unsuccessful attempts, with similar results, were made to maintain anaesthesia with cyclopropane, and the operation was eventually completed with nitrous oxide, oxygen, and ether and pethidine. During these periods of respiratory depression the pulse rate and blood pressure were relatively unaffected, although it was thought that temporary cardiac arrest had occurred earlier following endotracheal intubation. At the second-stage operation, one month later, cyclopropane was avoided and thiopentone, nitrous oxide, oxygen, pethidine, and alphaprodine ("nisentil") were given without any unusual effects.

Foster (1956a), from a review of the literature, suggests that irradiation around the head in appropriate doses may increase the permeability of intracranial vessels, and drugs which normally penetrate the blood–brain barrier may do so to a greater degree. The peculiar pattern of neuronal radiation damage seen suggests that excessive vagal tone may increase the hazards of intubation with cyclopropane, that consciousness may be more easily depressed, and that disturbances of temperature regulation may be encountered.

This case not only focuses attention on the potential hazards of deep *x*-ray therapy, but shows problems which may have to be faced following an atomic explosion. Whether penetration of relaxants across the blood–brain barrier occurs under these circumstances is not known, but the possibility should be kept in mind, especially if prolonged curarization is encountered (Foster, 1956b).

"Pitocin"

The intravenous use of the oxytocic principles of the pituitary gland is now an established practice in obstetrics. There are many reports of the dangers of administration where "pituitrin" and "pitressin" have been used. The pressor principles cause cardiac irregularities, hypotension, coronary constriction, and bronchospasm.

"Pitocin" is relatively free of vasopressin (but not completely so), and one would expect it to be less dangerous than the more impure preparations. However, Lesser and Eason (1954) have reported a death from the use of pitocin during emergence from light cyclopropane anaesthesia. They attributed this to the administration of vasopressin (although in a very dilute form) to a patient with impaired coronary circulation who was in a state of heightened vagal reflex activity associated with recovery from cyclopropane. It is important to note that the patient had recovered sufficiently to make purposeful movements of the arms, and that Parsloe *et al.* (1950) had previously shown that deep anaesthesia protects against arrhythmias and coronary constriction. It should also be mentioned that cardiac arrest occurred about one minute after starting the pitocin infusion and that necropsy revealed some degree of coronary artery disease.

Others

With some other drugs the relationship between the patient's condition and non-anaesthetic drugs is less obvious than with those already described. They should, however, be borne in mind.

Citrate Intoxication.—An increase in venous pressure with gradual onset of cardiac failure during massive transfusions may be due to this. It should be suspected if there is a poor response to apparently adequate blood transfusion, especially in patients with liver disease, during hypothermia, or where the hepatic circulation has been temporarily occluded. A death was reported from transfusion of 750 ml. of blood in the course of five minutes to a 4-months-old girl, and analysis showed that circulating blood had a citrate level equal to that of donor blood (*Curr. Res. Anesth.*, 1957). Bunker *et al.* (1955) recommend raising the level of ionized calcium by giving calcium chloride, in a 1% solution, 1 g. per 150 lb. (84 kg.) in 10–15 minutes as a priming dose, then 1 g. per hour as a continuous infusion. Firt and Hejhal (1957) recommend the concomitant use of procaine, and mention the important practical point that the calcium should never be given in the same transfusion bottle as the blood.

Obstetrics.—Failure of the baby to breathe after delivery may be attributed to the anaesthetic, especially if thiopentone is given, without any reference to previous analgesics. Roberts *et al.* (1957) have demonstrated the depressant effects of pethidine on foetal respiration, which may be very pronounced if the drug has been given to the mother less than three and a half hours before delivery.

Hypoxia.—Bedford (1955) has described the adverse effects of anaesthesia on old people. It does not seem to be realized that harm can be done to these patients by routine prescribing of large doses of morphine or other analgesics before or immediately after operation. Dementia is as likely to be due to hypoxia from such drugs as to any incident during the anaesthesia.

Summary and Conclusions

This paper draws attention to the increasing use in medicine over the past few years of drugs which influence the response of patients to anaesthesia. This side-action cannot usually be predicted by pharmacologists, and often it was detected only by chance when the preparation in question had been in clinical use for several years. In all the instances reported above the effect was to engender in patients an increase in toxicity of one or other of the effects of general anaesthetics.

Therapeutic agents whose main effect is to decrease vascular tone, such as the ganglion-blocking drugs or chlorpromazine, if given before anaesthesia, increase the hypotensive action of the narcotics, and severe and even fatal collapse may follow what are considered to be normal doses of anaesthetic drugs. This applies particularly to the intravenous barbiturate anaesthesia, where it is difficult, even in normal subjects, to predict the degree of hypotension that will follow injection and to adjust the dose so as to minimize this action. Care must also be taken in anaesthetizing patients who are receiving other hypotensive agents such as the rauwolfia or veratrum alkaloids or mecamylamine.

Clinical and experimental evidence shows that the phenothiazine derivatives prolong the narcotic action of anaesthetics. This also seems to apply to the non-phenothiazine preparations which are used for the control of tremor in Parkinsonism, and possibly may be a side-effect of all the tranquillizers.

A dangerous degree of respiratory depression can result from the combination of analgesic drugs and the intravenous barbiturates. A similar result can occur when cyclopropane is administered to patients who have had deep *x*-ray therapy to the head and neck.

Induced adrenocortical insufficiency, following the prolonged use of cortisone, its analogues, and corticotrophin, makes patients sensitive to the stress of surgery and anaesthesia. Prolonged severe hypotension, respiratory depression, and delayed recovery may follow surgical operations in such patients. These undue effects respond rapidly to intravenous cortisol, but prevention by increased pre-operative dosage of cortisone and corticotrophin is preferable. Increasing use of the steroids is focusing attention on this hazard, and especially so in minor cases, where one does not normally associate any risk with anaesthesia. It must also be stressed that steroid-induced primary pituitary failure may persist for several months after stopping the drugs.

The hazards of inducing anaesthesia in patients with a full stomach are now widely appreciated, and for this reason the pre-operative preparation of diabetic subjects with oral glucose is deprecated. Other problems which anaesthetists may encounter are the incompatibility of pitocin with light cyclopropane anaesthesia and the possibility of citrate intoxication as a differential diagnosis for cardiovascular collapse after massive transfusion of stored blood.

In very few of the cases reported did the anaesthetist know of the use of various drugs before operation, or associate hypotension or prolonged unconsciousness with any form of routine medical treatment. It is hoped that this publication will focus the attention of all medical practitioners on the fact that during anaesthesia unexpected adverse effects may be produced by drugs which do not appear to have any side-effects in the conscious subject. It is to be expected that many additions to the list of drugs discussed above will be noted in the future.

I am grateful to Professor C. A. Wells for permission to quote Cases 5 and 6, and to Dr. J. Cross for details of Case 7.

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At a meeting of the South-eastern Branch of the B.M.A. on June 23, 1858, Dr. H. R. SILVESTER gave the first account of his method of artificial respiration. After considering other methods already in use, including that introduced by Marshall Hall two years previously, he described his own, in which, with the patient in the dorsal position, the arms are pulled over the head to enlarge the capacity of the chest and induce inspiration, and are then returned to the sides to diminish the cavity of the thorax and produce forcible expiration, the whole process being repeated at the rate of 15 times a minute. Silvester's account was published in the *British Medical Journal* on July 17, 1858, at p. 576.

THE RISK TAKEN IN DRIVING UNDER THE INFLUENCE OF ALCOHOL

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Alcohol as a cause of accidents on the road has been widely studied. The investigations that have been carried out, valuable as they are, suffer, however, from a serious limitation. They have usually determined the effect of alcohol on the driver by measuring changes in his reaction time and in his skills, such as steering and braking (Smith, 1945; *Handbook*, 1952; Piret, 1952; Thompson, 1956). Large quantities of alcohol do, of course, produce deterioration in skill and reaction time, but the conclusion has too hastily been drawn that because no changes have been recorded after small quantities road safety is unaffected. This conclusion is not justified, for all that can be inferred from earlier inquiries is that these skills and reaction times are or are not affected. It cannot, for example, be inferred that a driver is not a menace on the road because his reaction times are unaffected or because a test of skill revealed no impairment. The decisive feature is not the driver's skill in itself but in relation to what he believes he could do and what he would in fact undertake. Thus the negative outcome of these studies may signify only that the methods of measurement were inadequate, not that the alcohol was without effect on the safety of the individual's driving.

Our aim, therefore, is to assess the effects of alcohol on the more complex psychological processes and performances involved in risks which drivers take and in hazards which they incur. By "risk-taking" we mean embarking on a task without being certain of success. There can be various degrees of certainty of success and hence varying degrees of risk-taking. By "incurring hazard" we mean embarking on a task in which the performer will not invariably succeed. Thus risk is measured by estimates of success before the task is attempted, whilst hazard is measured by the proportion of successes in actual performance (Cohen and Hansel, 1956). In our previous studies (Cohen, Dearnaley, and Hansel, 1955, 1956a) of risks and hazards taken by inexperienced and experienced drivers we found that, on the average, experienced drivers tended to (1) take less risk, (2) incur less hazard, (3) vary less in their driving behaviour, (4) be more realistic in judging their driving ability, and (5) be prepared to drive only when they felt secure and were in fact safe; on the other hand, an instructor with long experience drove without risk or hazard. That is to say, he never attempted a task unless he was sure he would succeed, and he never failed in any task which he undertook.

These results suggested that a comparison of drivers who had imbibed various quantities of alcohol with drivers free of alcohol might reveal similar differences. The present inquiry was designed to measure the influence of alcohol on those drivers who might be expected to show its effects least—namely, bus drivers of long

experience with records of safe driving. If any impairment due to alcohol could be demonstrated in such a group it would follow that the consequences might be far more serious in younger, less experienced, or less skilled drivers. We hoped that, by introducing psychological measures at once more sensitive and more fundamental in a general sense as well as in a sense specific to driving, any possible effects of smaller quantities of alcohol might reveal themselves.

Subjects and Procedure

Our subjects consisted of three groups of bus drivers working for the Manchester Corporation Transport Department. They had had on the average about 12 years' experience of driving a bus and, in addition, another eight years or so of driving other vehicles. The depots where the men worked were notified that the investigation was to take place, and drivers with awards for safe driving were invited to volunteer to take part. The arrangements were made through the personnel officer and representatives of the trade union. The average age of the men in each group was 45 years. There was one bachelor and one widower in the total sample; all except seven subjects had families. Drinking habits among the drivers varied from total abstinence to an average of 20 to 30 pints (11.5 to 17 litres) of beer a week; very few of our subjects drank spirits of any kind regularly.

All the drivers had worked an eight-hour morning shift immediately before the experiment and reported to us at 1 p.m. They then took lunch, without alcohol. During the meal they informed us about their drinking habits and driving experience. The alcohol, in the form of Scotch whisky (70° proof or 40% alcohol*), with an equal amount of soda-water, was taken from 2 to 2.30 p.m. The atmosphere was convivial.

The driving sessions began at 2.45 p.m. and lasted until about 3.15 p.m. The blood samples (0.5 ml.) were taken half an hour later. The procedure for the control group (without alcohol) was exactly the same as that for the two other groups except that they proceeded to the experiment immediately after the meal and the blood test was omitted. The moderate dose of whisky consisted of 2 British fl. oz. (or 56.8 ml.),† being the equivalent approximately of 23 ml. of *absolute alcohol*. The larger dose consisted of 6 British fl. oz. (170.4 ml.) of whisky, being the equivalent approximately of 68 ml. of *absolute alcohol*.

After consuming the whisky the drivers were taken to the site where the risk-taking experiments were to be conducted. The driver's task was to estimate how successful he would be in driving a bus through gaps of varying width. Having made his estimates he was to drive the bus through particular gaps.

Two vertical posts, 3 ft. (0.9 m.) high, 3 in. (7.6 cm.) square, and painted white, stood on a line. The gap between them could be varied and measured from calibrations on the line on which they were placed, the calibrations being visible only to the experimenter. Before the driving session began a bus 8 ft. (2.44 m.) wide was placed at a distance of 12 ft. (3.66 m.) from the gap and facing its centre.

The steps in the experimental procedure may be summarized as follows:

1. The driver sat in his seat and was told that he was shortly to drive his bus between the two posts in front of him. First, however, he was to tell us how well he *thought* he could do this at different sizes of gap between the two posts. At each prearranged size of gap between the posts the driver was asked to say how many times out of five he thought he could drive through without touching the posts. The gap between the posts was increased by intervals of 2 in. (5 cm.), beginning with a gap of 7 ft. 4in. (2.23 m.) or smaller if a driver thought he could drive through this gap. This was continued until the driver said he could succeed five times out of five.

2. We next determined the least size of gap through which the driver would *actually attempt* to drive. Here, too, the posts were moved apart in stages except that the gap was now increased by intervals of 1 in. (2.5 cm.) at a time. The size of the gap between the posts was increased until the driver signalled his intention to drive through it. He attempted to do so without touching the posts and then drove round the training site so as to return to the starting-point. He drove at his own speed.

3. Finally, we measured the driver's performance at different sizes of gap. The gaps through which he was asked to drive his bus were such as to reveal the smallest gaps at which he would succeed (*a*) once or twice out of five, (*b*) three or four times out of five, and (c) five times out of five.

The experiments was carried out at the Training School for Bus Drivers of the Manchester Corporation Transport Department.

Before presenting the results, we wish to make certain comments on the above procedure. First, it might be asked whether different estimates might be obtained if our subjects were asked to say how many times, say, out of ten (or a hundred) they would succeed. We have shown elsewhere (Cohen *et al.*, 1956b) that the mean estimates of adults, when expressed as fractions of unity—that is, as subjective probabilities—are unaffected by the range within which they are made. Thus estimates made within one range are transposable to another. Secondly, it might be asked whether the estimates would differ if the subjects had to say how many times they would fail rather than how many times they would succeed. Here, too, we have shown (Cohen *et al.*, 1957) that, at any rate, when the range is "out of five," estimates of success and estimates of failure appear to be additive.

A third point arises in connexion with the order in which the estimates were made. For practical reasons, it was only convenient to present the entire series of gaps in *ascending* order of magnitude. In principle it would have been equally possible to present them in *descending* or random order of magnitude. The ascending order, as we know from our previous experiments (Cohen *et al.*, 1958), has the effect of yielding larger estimates for each gap (or level of difficulty) than the descending order. The ascending order of presentation was also employed in relation to the least gap which the driver was prepared to attempt. This feature of the procedure must be borne in mind when considering the results.

Results

1. Hazard

The first results which we wish to present reveal the greatest degree of hazard in which our three groups of drivers became involved. This is indicated by the difference between the mean of the narrowest gap which the drivers attempted and the mean of the narrowest gap through which they were always able to drive successfully, as shown in Table I.

TABLE I.—*Margins of Hazard (Means)—Width of Bus=8 ft. (2.44 m.)*

Quantity of Whisky (1)		Narrowest Gap which Drivers Attempted (2)		Narrowest Gap at which Drivers Always Succeeded (3)		Difference (Margin of Hazard) (4)	
British fl. oz.	ml.	ft. in.	m.	ft. in.	m.	in.	cm.
0	0	7 11·3	2·420	8 6·7	2·610	−7·4	−18·8
2	56·8	7 9·6	2·375	8 6·9	2·615	−9·3	−23·6
6	170·4	7 7·8	2·330	8 7·3	2·625	−11·5	−29·2

On the average, the drivers in all three groups were prepared to drive an 8-ft. (2.44-m.) bus through a gap less than 8 ft. in width, the proportions in each group undertaking this being 68, 75, and 80% respectively. Under our experimental conditions, therefore, even the alcohol-free

*In the United States the *degrees proof* is twice the percentage of alcohol by volume. So that in the U.S. this whisky would be described as 80° proof.

†The U.S. fluid ounce (29.6 ml.) is rather larger than the British (28.4 ml.).

drivers were involved in hazard. The effect of the alcohol is, however, revealed in the degree of hazard incurred by the drivers in the three groups. Three inferences relating to the effect of alcohol may be drawn from Table I. First, as the drivers consumed more whisky they were prepared to drive through a narrower gap. Second, as they consumed more whisky they needed a wider gap before they could always succeed; thus there was a progressive deterioration in performance as more whisky was consumed. Third, it follows that the margin of hazard, as shown in the fourth column, increases with greater intake of alcohol. The difference between the two extreme groups is significant ($t=2.2$, $df=37$, $p<0.05$). We may therefore conclude that, as compared with the alcohol-free drivers, those who had taken 6 fl. oz. of whisky (68 ml. of absolute alcohol) were involved in considerably greater hazard.

2. Risk

Whilst greater hazards were incurred by imbibing alcohol, the risks taken were unaffected. In other words, although the drivers were prepared to drive through a narrower gap, their confidence of success at this gap remained unchanged. At the narrowest gap which they attempted the mean estimates of success of the groups taking 0, 2, and 6 fl. oz. respectively were 2.8, 2.1, and 2.8 times out of five. We can express these as subjective probabilities by converting them to fractions of unity, thus: 0.56, 0.42, and 0.56 respectively. These values do not differ significantly. Accordingly the effect of alcohol was not to make drivers take more risk—that is, act at a lower level of subjective probability—but to assign the same subjective probability to a more difficult task. If the difficulty of the task remained unchanged they became more optimistic and attached a higher subjective probability to the task.

Furthermore, on the average, the narrowest gap (7 ft. 10.5 in.—2.40 m.) at which the high-alcohol group believed they could always succeed was smaller than the narrowest gap (7 ft. 11.3 in.—2.42 m.) which the alcohol-free drivers even ventured to attempt.

Alcohol thus produced dangerous effects apart from inducing the drivers to incur greater hazards. In addition to influencing the drivers to attempt to drive through a narrower gap, it also induced greater confidence of success at a narrower gap. This may be seen from column 3 of Table II. To illustrate: the subjective probability of the high alcohol group for a gap of 7 ft. 7.8 in. (2.33 m.)—the narrowest they attempted—was 0.56, as compared with 0.34 for the non-alcohol group. Similarly, because the values in both column 2 and column 3 of Table II decline with increasing alcohol, the margins of safety remain more or less the same, the small variations in column 4 not being significant.*

TABLE II.—*Margins of Safety (Means)*

Quantity of Whisky (1)		Narrowest Gap which Drivers Attempted (2)		Narrowest Gap at which Drivers *Believed* They Would Always Succeed (3)		Difference (Margin of Safety) (4)	
British fl. oz.	ml.	ft. in.	m.	ft. in.	m.	in.	cm.
0	0	7 11·3	2·420	8 1·3	2·470	−2·0	−5·1
2	56·8	7 9·6	2·375	8 1·4	2·475	−3·8	−9·6
6	170·4	7 7·8	2·330	7 10·5	2·400	−2·7	−6·9

3. Estimates and Performance

The effect of alcohol may be shown in a third manner (as in Table III), by comparing the size of the gap at which the drivers believed they would always succeed with the gap at which they did in fact always succeed.

*The effect on speed of driving is similar. As Vernon (1936) has shown, moderate quantities of alcohol tend to make most drivers increase their rate of driving, this tendency being usually unrecognized by them.

TABLE III.—*Estimates in Relation to Performance (Means)*

Quantity of Whisky (1)		Narrowest Gap at which Drivers *Believed* They Would Always Succeed (2)		Narrowest Gap at which Drivers Always Succeeded (3)		Difference (4)	
British fl. oz.	ml.	ft. in.	m.	ft. in.	m.	in.	cm.
0	0	8 1·3	2·470	8 6·7	2·610	−5·4	−13·7
2	56·8	8 1·4	2·475	8 6·9	2·615	−5·5	−14·0
6	170·4	7 10·5	2·400	8 7·3	2·625	−8·8	−22·4

In the circumstances of this experiment even the drivers in the control group displayed an excess of confidence. They believed they would succeed before they could actually succeed. But this effect was much more marked in the group which had taken 6 fl. oz. of whisky. The influence of the alcohol thus led to a tendency to overrate ability in relation to performance, even in our group of experienced drivers. The fact that two whiskies had little or no affect on our highly selected group should by no means encourage any ordinary driver to indulge himself to that extent or less.

4. Blood Alcohol in Relation to Whisky Consumed

Analysis* of the blood samples showed that the mean level of blood alcohol was 0.04 mg./ml. ($\sigma=0.07$) in the group taking 2 fl. oz. of whisky (=23 ml. of absolute alcohol) and 0.58 mg./ml. ($\sigma=0.17$) in the group taking 6 fl. oz. (=68 ml. of absolute alcohol). The difference between these two means is significant ($t=12.5$, $df=38$, ($p<0.001$). With one exception it is possible to state from a knowledge of his blood alcohol whether a driver had taken 2 or 6 fl. oz. of whisky. It follows that the mean level of blood alcohol in the two groups is related to their respective mean margins of hazard. But the variation in the margin of hazard *within* the groups is so large as compared with the variation *between* them that a knowledge of the blood alcohol of any individual driver tells us little about the degrees of hazard in which he might become involved.

Discussion of Results

It is a well-known fact that individuals vary widely in their reaction to the same amount of alcohol. Our results bear this out. Some of our subjects seem to have been more adversely affected by two whiskies than others by six. Hence, so far as the practical implications of this investigation are concerned, we have to bear in mind not only deterioration in the average performance of drivers in general after taking alcohol, but also extreme effects on a small proportion of individuals.

After taking alcohol certain drivers attempted to drive through extremely narrow gaps. No alcohol-free driver tried to drive his 8-ft. (2.44-m.) bus through a gap less than 7 ft. 5 in. (2.26 m.) in width, whereas three of the

*We are most grateful to Dr. L. P. Kendal, M.Sc., senior lecturer in physiological chemistry at the University of Manchester, for carrying out the analysis of the blood samples. Dr. Kendal has kindly provided the following note on the method employed of estimating the blood alcohol concentration: "The highly specific alcohol dehydrogenase method was used (Bücher and Redetzki, 1951; Bonnichsen and Theorell, 1951); and the instructions given in the pamphlet published by C. J. Boehringer and Soehne, of Mannheim, from whom diphosphopyridine nucleotide and crystalline alcohol dehydrogenase (yeast) were purchased, were followed. At the testing-ground a blood sample of approximately 0.5 ml. was withdrawn from the subject into a syringe by venepuncture, and transferred immediately into a weighed bottle containing 4 ml. of the perchloric acid protein precipitant. The bottle was reweighed on its return to the laboratory and the weight of blood obtained by difference. The volume of the blood sample was then calculated on the assumption that its specific gravity was 1060. The well-mixed contents of the bottle were then transferred to a centrifuge tube, and, after centrifuging, the ethanol concentration in the clear centrifugate was determined, always in duplicate, by the alcohol dehydrogenase-DPN spectrophotometric method. From the mean of the duplicates the ethanol concentration in the original blood sample was calculated."

group taking 2 fl. oz. (56.8 ml.) were prepared to undertake this task, one of them being willing to attempt a gap 1 ft. 2 in. (35.5 cm.) narrower than his bus, his subjective probability of success at this gap being 0.8, although his blood alcohol was only 0.02 mg./ml. Two drivers after 6 fl. oz. (170.4 ml.) attempted gaps which were respectively 1 ft. 2 in. (35.5 cm.) and 1 ft. 4 in. (40.6 cm.) narrower than the bus; the blood alcohol of the former was 0.74 mg./ml. and of the latter 0.26 mg./ml., and the subjective probabilities of success were 0.6 and zero respectively.

It is perhaps not surprising that in our very highly selected and experienced sample of drivers there should have been one or two who compensated for the effects of six whiskies by becoming extremely cautious. One driver, after 6 fl. oz. (170.4 ml.) of whisky, refrained from making an attempt until the gap was 10 in. (25.4 cm.) wider than his bus, though he *believed* he could always succeed when the gap was 8 in. (20.3 cm.) wider, and, in fact, he always succeeded when it was 7 in. (17.8 cm.) wider; his blood alcohol was as much as 0.60 mg./ml. The blood alcohol of the most dangerous driver was less than half that of the most cautious one. This relatively dangerous driver was 5 stone (31.8 kg.) heavier and 15 years older than the cautious one, though a greater weight and age might be expected to be associated with a reduced effect of alcohol. The absence of any significant correlations between performance and the age, weight, driving experience, and drinking habits of our drivers may be attributed to the homogeneity of the sample.

The reader may wonder whether our results suggest any level of blood alcohol which should not be exceeded. In the United States, the National Safety Council (1953) recommended that the lines of demarcation between levels of blood alcohol should be as follows:

0.0–0.5 mg./ml.,	safe				
0.5–1.0	„	„	possibly	under influence of alcohol	
1.0–1.5	„	„	probably	„	„ „
Above 1.5	„	„	definitely	„	„ „ „

We do not, however, think it is justifiable, on the basis of our experiment, to establish the interval of 0.0–0.5 as safe. We have found that the trustworthiness of a man's judgment of his driving skill was impaired even after a small quantity of alcohol producing a blood alcohol concentration lower than 0.5 mg./ml. This impairment of judgment occurred in what might be described as the *élite* of drivers on the road. Furthermore, the effects of the alcohol were in a sense minimal, as the alcohol was taken immediately after a meal. The performance of the drivers deteriorated, they were involved in greater hazards, and they displayed a false confidence in their driving abilities.

Ordinarily a driver suspected of being under the influence of alcohol cannot be given a test of safe driving. We suggest, therefore, that measures taken to reduce traffic accidents due to alcohol must forbid the taking of alcohol for some specified period before driving. The menace to public safety comes particularly from those who, after a slight amount of alcohol, feel they are sober or believe they are driving more cautiously.

In Great Britain it is extremely difficult to assess the effects of alcohol on the incidence of traffic accidents. The reason is that the police, when reporting an accident, are extremely reluctant to state that they strongly suspect the driver of being under the influence of alcohol unless they charge him with being drunk. It is well known that the police are very unhappy about this state of affairs. They are well aware that even when the driver is charged with being drunk he stands a good chance of being acquitted if he elects to go for trial before a jury at quarter sessions.

We have been privately told by many members of the police force that they have no confidence in the tables published by the Ministry of Transport and Civil Aviation and Scottish Home Department (1955–7), giving details of the "factors where drivers were regarded by the police as contributing to the accident." From the figures in these tables the influence of alcohol appears to be a negligible factor, whereas the police believe that the figures give a grossly misleading impression. Thus, for example, in 1956 there were 216,172 road accidents in Great Britain. "The influence of drink or a drug" was considered by the police (according to the official report) to be a contributing factor in only 994 of these accidents—that is, less than 0.5%. In 1954 and 1955 the proportion was approximately the same. The true proportion, according to various estimates and investigations in different countries, would appear to be of the order of 50%. The position appears to be much the same in many other countries. According to Piret (1952) there appears to be a conspiracy of silence between the authorities, the lawyers, and the witnesses to wrap the effects in a cloak of innocence. Only the most drastic measures, firmly carried out, could cope with this appalling state of affairs.

Conclusion

Our main results may be briefly summarized as follows.

Drivers who took alcohol became involved in greater hazards than alcohol-free drivers.

As the amount of alcohol taken was increased, the drivers were prepared to drive their vehicles through narrower gaps. This revealed that the alcohol had adversely affected their judgment.

The performance of the drivers, as well as their judgment, progressively deteriorated as they consumed more alcohol.

After taking alcohol the drivers became more dangerous, although they did not take greater risks. This was due to the fact that the level of confidence above which they were prepared to drive their bus remained unchanged. But at any given size of gap the drivers, after taking alcohol, were more confident of success. Thus they were prepared to drive through narrower gaps.

Alcohol intensified any driver's tendency to overrate his ability in relation to his performance.

APPENDIX 1

Margins of Hazard (*Standard Deviations*)

Quantity of Whisky (1)		Narrowest Gap which Drivers Attempted (2)		Narrowest Gap at which Drivers Always Succeeded (3)		Difference (Margin of Hazard) (4)	
British fl. oz.	ml.	in.	cm.	in.	cm.	in.	cm.
0	0	5·5	14·0	1·8	4·6	5·4	13·7
2	56·8	5·3	13·5	1·4	3·6	5·0	12·7
6	170·4	6·0	15·2	1·7	4·3	5·8	14·7

Margins of Safety (*Standard Deviations*)

Quantity of Whisky (1)		Narrowest Gap which Drivers Attempted (2)		Narrowest Gap at which Drivers *Believed* They Would Always Succeed (3)		Difference (Margin of Safety) (4)	
British fl. oz.	ml.	in.	cm.	in.	cm.	in.	cm.
0	0	5·5	14·0	6·3	16·0	4·4	11·2
2	56·8	5·3	13·5	7·9	20·0	4·6	11·7
6	170·4	6·0	15·2	5·6	14·2	5·4	13·7

APPENDIX 2

Driving under the Influence of Drink of Drug

The British reader might be specially interested in the statistical differences between the proportions convicted of (*a*) those who elect to be dealt with by magistrates and

(*b*) those who elect to go for trial, respectively. Relevant figures for the years 1953 to 1957 have very kindly been provided for the County of Lancashire by the Chief Constable, Colonel T. E. St. Johnston. These are summarized below:

	Electing to be Dealt with by Magistrates (1)	Percentage Convicted (2)	Electing to go for Trial (3)	Percentage Convicted (4)	Percentage of Total Charged who Elect to go for Trial (5)
1953	115	92	8	38	6
1954	161	94	20	35	11
1955	166	92	13	46	7
1956	197	89	30	33	13
1957	193	91	37*	35	20

* Excluding 10 who elected to go for trial but not yet tried.

It might be argued that those electing to go for trial are in fact less culpable. If this is not the case, the more or less constant differences between columns (2) and (4) require some explanation. From column (5) it may be seen that there is a tendency for an increasing proportion of the total charged to elect to go for trial. This is not surprising if it is becoming more widely believed that trial by jury, other things being equal, carries a higher probability of acquittal. But it is hardly credible that an increasing proportion of those less culpable are being apprehended by the police and electing to go for trial. These figures bring to light what appears to be a serious discrepancy in the administration of the law. We are faced with one of two conclusions: if both groups (columns 1 and 3) are equally culpable, which may well be the case, either a large number of people are wrongly convicted by the magistrates or wrongly acquitted by the jury.

We should like to express our gratitude to the Manchester Corporation Transport Department, and in particular to Mr. J. F. J. Webb, personnel officer, and Mr. G. Walker, chief instructor, for their most valuable help in making this investigation possible. Our thanks are also due to Dr. R. I. Johns and Sister E. West for taking the blood samples, and to the local branch of the Transport and General Workers' Union and the volunteer drivers for their helpful co-operation.

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The American Heart Association (44, East 23rd Street, New York) has issued a booklet summarizing, in easily understood diagrams, various mortality statistics for the U.S.A. As elsewhere, deaths from rheumatic heart disease have fallen sharply in the last two decades, though it still causes 31% of the deaths from cardiovascular disease among young people aged 5–24. A comparison of death rates from cardiovascular disease in different countries among men aged 45–64 in the year 1954 shows it to be greater in the U.S.A. than in most of the countries of Europe, including the United Kingdom, and about double the rates in the Scandinavian countries, France, Italy, the Netherlands, and the German Federal Republic.

URINE-ALCOHOL TESTS AND "DRUNK-IN-CHARGE": SURVEY OF 312 CASES

BY

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This laboratory has during the past few years made several hundred alcohol determinations on blood and/or urine samples taken from allegedly intoxicated drivers. This number seems to me large enough for a statistical examination of the results to be of interest.

TABLE I

Concentration in Urine* (mg./100 ml.)	No. of Cases	Circumstances: Accident†	Circumstances: No Accident	Circumstances: Not Driving	Medical Opinion: Unfit	Medical Opinion: Borderline‡	Medical Opinion: Fit	Result of Proceedings: Convicted	Pleaded Guilty	Acquitted	Convicted of Other Offence§	No Action Taken
Under 100 ..	1	1									1	
101–120 ..	3	3			2	1		1		1		1
121–140 ..	6	3	1		3	1		4		2		
141–160 ..	2	1	1		2			1	1			
161–180 ..	4	4			2			1	1	1		
181–200 ..	9	5	1	1	1	2	3	2	1	3		3
201–220 ..	15	7	4	2	5	6	1	4	4	2	2	3
221–240 ..	26	11	7	4	20	2		12	6	3	3	2
241–260 ..	24	12	7		14	2	1	12	6	3	1	2
261–280 ..	29	5	13	6	17	4		17	7	5		
281–300 ..	47	20	15	6	35	4		18	17	8		1
301–320 ..	25	14	3	6	14	2	2	12	6	6		1
321–340 ..	24	4	11	2	14	1	1‖	8	7	5	3	1
341–360 ..	31	8	11	8	23	4		12	13	3	1	1
361–380 ..	22	6	7	3	14	1	1‖	11	8	2	1	
381–400 ..	19	7	7	1	14	1		7	7	4		
401–420 ..	14	4	3	4	7			10		2		1¶
421–440 ..	4	2		1	3			1	1	1		1••
441–460 ..	3	1		2	2	1		3				
461–480 ..	2		1		1				2			
481–500 ..	1		1		1			1				
Over 500 ..	1	1							1			

* In the few cases in which only blood samples were analysed the blood concentrations have been included here after multiplication by 4/3.
† Incidents involving personal injury, damage to other vehicles, driving off the road so as to be unable to proceed, motor-cyclists falling off, etc. Mere temporary mounting of road verge, etc., not counted as accidents.
‡ Inconclusive opinions such as: "recovering from effects of alcohol at time of examination," "unable to distinguish between effects of alcohol and shock," etc.
§ Conviction of other traffic offences in which element of intoxication does not enter.
‖ Defendants convicted in spite of medical opinion.
¶ Defendant committed suicide.
•• Defendant certified insane.

The Investigation

In all, 312 cases are considered; the details are summarized in Table I. The figures under the headings "circumstances," "medical opinion," and "result of proceedings" are based on information supplied by the police forces which submitted the samples. Where the sum of the numbers under each of these headings is less than the total number of cases in the same concentration range, that signifies in most cases merely that the relevant information could not be obtained. In a small number of cases, however, the defendants were not medically examined.

Over 90% of the samples consisted of urine only. Where both blood and urine samples were submitted, only the urine figures are included in Table I; they are probably in general more significant than figures for blood taken, usually, at least an hour after the defendant was arrested. Where only blood samples were submitted, however, the figures have been included in the table after multiplication by 4/3.

The ratio 4:3 (1.33:1) for urine:blood alcohol appears to be generally accepted (*Taylor's Medical Jurisprudence*, 1957), although Elbel and Schleyer (1956) suggest that the

true figure may be slightly lower—namely, about 1.25. In the few cases considered here in which both blood and urine samples were submitted, the ratio found never fell significantly below 1.33 (the lowest being 1.27), but sometimes considerably exceeded it. This could reasonably be attributed in all cases to an unusually long interval, without the passage of urine, between drinking and collection of samples. In such circumstances the concentration in the urine will depend (neglecting reabsorption), not on that in the blood at the time of sampling, but on the average in the blood over a period of falling alcohol concentration; this average will of course be higher than the concentration at the end of the period.

It will be seen from Table I and Fig. 1 that the peak of "police attention" occurs at a concentration of about 0.30% w/v (300 mg./100 ml). This is in complete agreement with the result found by Nickolls (1956) in a series of 1,000 cases. The mean figure for all the cases considered here is in fact 0.300% precisely, and the median 0.294%; 84% of the cases lie within the concentration range 0.20–0.40%. Although the cases cover a period of 10 years, the means for successive shorter periods within the whole show no significant differences or apparent trend.

If only the cases in which the defendant was actually driving are considered, one could on common-sense grounds expect the mean concentration in accident cases to be lower than that in no-accident ones. The obviously drunk driver is most commonly stopped before he has gone very far—that is, there is a good chance that he will be stopped before he has hit anyone or anything. On the other hand, the driver who shows no gross signs of intoxication is not so liable to attract the unfavourable attention of the police unless he is involved in an accident.

Table II and Fig. 2 show that this expectation is borne out. It is also confirmed by statistical calculation. The mean concentration in 116 cases in which accidents occurred is 0.284%; that in 91 cases without accidents is 0.308%. The standard deviations are 0.082 and 0.064 respectively, and the standard error of the difference 0.010. As this last figure is less than half the difference between the means (0.024), the difference is significant at the 0.05 level of probability (Chambers, 1952a)—that is, the odds in favour of the difference being real, and not simply the result of random variation, are at least 19 to 1.

As is only to be expected, the proportion of drivers definitely considered unfit on medical examination rises with increasing alcohol concentration (Table II). A 2 by 6 contingency table of the medical opinion figures in Table II gives $\chi^2=10.3$. This is significant at the 0.10 level of probability, but not at the 0.05 level. The figures in Table II, however, suggest that above a certain critical concentration the proportion of drivers pronounced unfit remains approximately constant, and possibly depends on factors other than an objective assessment of the defendant's condition. A series of 2 by 2 contingency tables, using the numbers of cases above, and below, various concentration levels, gives the greatest values of χ^2 when the dividing line is taken at 0.220% (χ^2 then $=24.3$, applying Yates's correction (Chambers, 1952b)). This suggests that the critical concentration mentioned above lies at about this level. It may be noted that it is close to the blood-alcohol level of 0.15% which, following the pre-war investigations in the U.S.A. (Committee to Study Problems of Motor Vehicle Accidents, 1937), is widely held to be an average dividing line between possible and certain unfitness to drive.

TABLE II.—*Distribution of Cases Among Various Categories*

Concentration Range (mg./100 ml.)	Circumstances: Accidents	Circumstances: Driving Without Accident	Circumstances: Accidents/Total Driving Cases (As percentage: to nearest 5%)	Medical Opinion: Unfit to Drive	Medical Opinion: All Others	Medical Opinion: Unfit/Total Cases (As percentage: to nearest 5%)	Result of Proceedings: Convictions (Including Guilty Pleas)	Result of Proceedings: All Others	Result of Proceedings: Convictions/Total Cases (As percentage: to nearest 5%)
Under 200	17	3	85	10	7	60	12	12	50
201–250	23	16	60	32	10	75	35	17	65
251–300	31	29	50	59	9	85	67	17	80
301–350	22	22	50	43	7	85	48	20	70
351–400	18	18	50	36	7	85	44	9	85
Over 400	8	5	60	14	1	95	19	5	80

The totals in the second and third categories are: 194 unfit to drive in 235 cases (83%), and 225 convicted or pleaded guilty in 305 cases (74%).

The proportion of drivers convicted also naturally rises with increasing alcohol concentration (Fig. 3). An attempt was made to discover whether there is any direct connexion between these two variables by considering only cases which were medically considered unfit to drive and in which "not guilty" pleas were entered—that is, cases in all of which the medical evidence was unfavourable to the defendant and the courts had to reach a decision on the evidence before them. The figures for these cases are given in Table III.

TABLE III

	Range of Urine-Alcohol Concentrations (mg./100 ml.)			
	Under 250	251–300	301–350	Over 350
Cases convicted after pleading not guilty (mean concentration 0·301%) ..	21	31	16	26
Cases not convicted (mean concentration 0·307%) ..	6	8	10	8

A 2 by 4 contingency table of the figures in Table III gives a value of χ^2 which is not significant even at the 0.50 level. (It will also be seen that the mean concentration for the cases not convicted is in fact slightly higher than that for those convicted; the difference is, however, statistically not significant.) That is, the results available suggest that

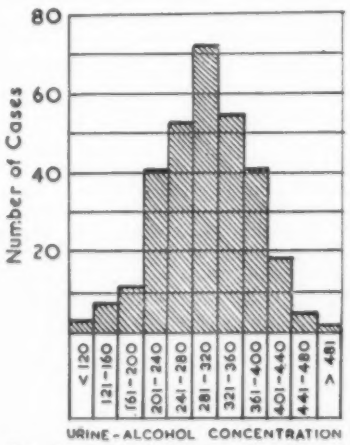

FIG. 1.—Urine-alcohol concentration at which the peak of "police attention" occurs.

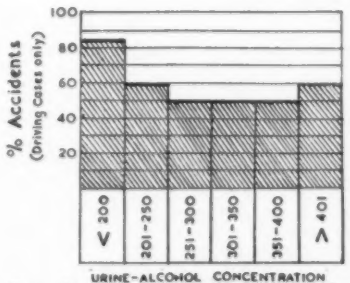

FIG. 2.—Percentage of accidents in relation to urine-alcohol concentration.

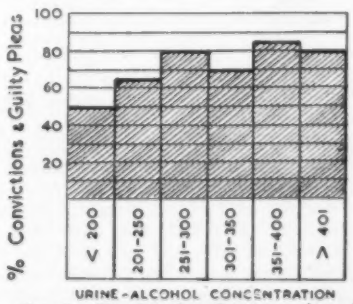

FIG. 3.—Showing that the proportion of drivers convicted rises with increase of alcohol concentration.

the courts, in reaching their decisions, were not influenced at all by evidence of urine-alcohol concentrations. Clearly, however, this conclusion can only be tentative at this stage. To test it more strictly, more account would have to be taken of other factors influencing the decisions; to do this it would be necessary to consider a much larger number of cases.

Finally, attempts were made by constructing 2 by 2 contingency tables to find whether there was any relationship between the occurrence of accidents on the one hand and the plea of the defendant or the decision of the court on the other. Again only cases medically pronounced unfit to drive were considered. There appeared to be no significant relationship whatever. That is, whether or not an accident had occurred appeared to have no bearing on the probability of the defendant pleading guilty, or on the decision of the court if he pleaded not guilty.

All of the cases considered here came from south-west England. It would be interesting to see a similar analysis for a comparable or, preferably, larger series of cases from the whole country, or at least from other regions of it.

Summary and Conclusions

The urine-alcohol concentrations of persons arrested for driving whilst under the influence of drink appear to be normally distributed around a mean value of 300 mg./100 ml.

The mean figure for cases in which accidents occurred is significantly lower than that for cases in which the defendants were driving without accident.

The probability of the defendant being medically pronounced unfit to drive rises with increasing urine-alcohol concentration up to a figure of about 220 mg./100 ml., but above this figure appears to be about the same for all concentrations.

The statistical evidence available suggests that the decisions of the courts are not influenced at all by legal evidence of urine-alcohol concentrations.

The statistical evidence available also suggests that there is no relationship between the incidence of accidents and the pleas of the defendants or decisions of the courts.

I thank Mr. E. B. Parkes, Director of this Laboratory, for permission to publish this paper, and Dr. Frank George, University of Bristol, for advice on statistical methods.

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Nursing for Men is a new title in the "Choice of Careers" booklets issued by the Central Youth Employment Executive. It describes nursing for men in and outside hospitals, training, conditions of service, and openings and prospects. Mental and mental deficiency nursing were the first branch of the profession in which men could qualify, and these still offer the best opportunities for the male nurse, states the booklet. The first male nurse was accepted for general training in 1930, and now there are many hospitals where they can receive training. This booklet is prepared by the Ministry of Labour and National Service and the Central Office of Information. It is obtainable from H.M.S.O., price 1s. 6d. net.

EXPERIMENTAL INVESTIGATION OF THE RELATIONSHIP BETWEEN METHOD OF TREATMENT AND SUBSEQUENT IMMUNITY*

BY

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Although children with acute respiratory infection respond well to a single large dose of penicillin or sulphonamide (Platt, 1940; Lauria, 1947; Wilken-Jensen, 1948; Friderichsen and Walther, 1950; Jersild *et al.*, 1956; Joseph, 1958), it is not known whether the immunity following this method of treatment differs from that following repeated chemotherapy. This treatment with a single large dose has been called stosstherapy by Gaisford (1951), a name originally given by Harnapp (1938) to a method of treatment of rickets with a single massive oral dose of vitamin D.

Good immunity in rabbits and mice developed following sulphapyridine treatment of pneumococcal infection (Whitby, 1938a; Larson *et al.*, 1939; Curnen and MacLeod, 1942). This immunity was the same in quantity, quality, and speed of production as that created by orthodox active immunization (Whitby, 1938b), and the degree of immunity was related quantitatively to the size of the infecting dose (McIntosh and Whitby, 1939).

The action of penicillin, however, differs from that of sulphonamide, and immunity following treatment with penicillin may be different. McIntosh and Whitby (1939) showed that sulphapyridine exerted its bacteriostatic action only after a lag of several hours, thus allowing time for the formation of antibody, whereas MacLeod and Stone (1945) have pointed out that by contrast the action of penicillin was immediate and might be independent of an immune response. Thus Harrison (1946) showed that, when penicillin was given to rabbits four hours after infection, no antibody response could be detected; when he reinfected his survivors all the animals previously saved by penicillin died in five to six days as compared with controls, which died in 36 hours. By contrast, rabbits saved by penicillin given 24 hours after infection, when reinfected, survived and showed a high titre of antibodies. Harrison (1946), with mice, and Skinsnes and Woolridge (1948), with protein-depleted rats, obtained similar results.

Present Investigation

White male mice of Parkes A strain were used. They were infected with a known dose of type I pneumococci (NCTC 7465), and divided into three groups: (1) single dose (stoss), (2) repeated doses, and (3) untreated. Ten days after the original infection, the survivors in groups 1 and 2, and a new control group, were each infected with a challenging dose of pneumococci, and the degree of immunity was measured by mortality.

My preliminary experiments showed that the optimum interval between infection and treatment was 10 hours, which agrees with the findings of Harrison (1946) and Skinsnes and Woolridge (1948). Too high a mortality resulted if the mice were left untreated for longer periods.

*Based on M.D. thesis for University of Cambridge, 1957.

Treatment.—Although studies of the combination of sulphonamide and penicillin *in vitro* (Ungar, 1943; Rammelkamp and Keefer, 1943; Bigger, 1944b; Garrod, 1944; Kirby, 1944; Hobby and Dawson, 1944) or *in vivo* (Sultan *et al.*, 1945; Nitti *et al.*, 1946) have not shown clear-cut results, such a combination was used in these experiments in order to resemble common clinical practice. The dose of both penicillin and sulphadimidine was calculated on body weight, and was proportional to that usually given to a child. For 20-g. mice the single dose was 600 units of penicillin and 6 mg. of sulphadimidine, and the repeated dose was 100 units of penicillin and 1.3 mg. of sulphadimidine eight-hourly for six doses.

The size of the challenging dose also had to be gauged by preliminary experiment. The aim was to achieve a mortality of between 50% and 100% of controls, which allowed differences to appear between the groups of treated animals. In all experiments except one the challenging doses were of two strengths so as to facilitate distinction between the treated animals.

Methods

Seven experiments consisting of the primary infection and its treatment were performed, each using 150 mice (and on one occasion 180). There were 13 reinfection experiments, because with one exception the survivors from the primary infection were divided into two equal groups and reinfected with two different challenging doses. The experiments followed the same pattern, but the size of both the primary and the challenging infecting dose varied, so that the results were reasonably broad. The pneumococci were frequently passaged through mice, but an unusually large number of organisms had to be injected to produce the mortality needed.

On the day before the experiment an infected mouse was killed and heart blood was streaked on blood agar and incubated. Eighteen hours later a glucose-broth culture was prepared from the agar and was incubated for six hours. This broth was serially diluted, colony counts were made, and doses of 0.2 ml. were injected intraperitoneally in mice. The 150 infected mice were left untreated for 10 hours. Preliminary experiments had shown that blood cultures were positive at this time. Fifty mice were then given only one injection of a freshly prepared mixture of 600 units of sodium penicillin and 6 mg. of sodium sulphadimidine. A further 50 mice were injected with a mixture of 100 units of sodium penicillin and 1.3 mg. of sodium sulphadimidine, and this was repeated for six doses at eight-hourly intervals. The remaining 50 infected mice were left untreated.

The three groups of mice were observed for the next ten days, and the heart blood and peritoneal exudate of the treated animals that died were cultured. At the end of this period the survivors in each group, and a fresh group of 50 controls, were reinfected with pneumococci intraperitoneally, prepared as for the initial infection. The actual dose varied with the experiment. The animals were left untreated and the mortality and day of death noted; the heart blood and peritoneal exudate of those that died after the third day were cultured.

Colony counts were done by the method of Miles *et al.* (1938). Counting was made easier by staining with Janus green (Joseph and Mann, 1958) and using a graticule and binocular microscope.

Results: Primary Infection

Experiment 4 has been selected as representative and is described in detail. The differences found in the other experiments are pointed out below.

Experiment 4

Three groups (each of 50 mice) were injected intraperitoneally with 0.2 ml. of a 1 in 100 dilution of a six-hour glucose-broth culture of pneumococci (about 750,000 organisms). One animal in the stoss group died a few minutes after the injection; post-mortem examination did not reveal the cause of death. This death has not been recorded as due to pneumococcal infection. Ten hours later about two-thirds of the animals looked ill, had ruffled coats, and were sluggish and unresponsive. Some of the others showed these signs to a lesser degree. At this time the 49 in the stoss group received an intramuscular injection of 600 units of sodium penicillin and 6 mg. of sodium sulphadimidine in 0.3 ml. of sterile water, and the 50 in the repeated group 100 units of sodium penicillin and 1.3 mg. of sodium sulphadimidine. Fifty animals were left untreated.

This first treatment was given at midnight; progress was next observed eight hours later, when the repeated group received a further injection. At this stage the change in the mice was remarkable; all in the stoss and most in the repeated groups were lively, alert, and had smooth coats, and only a few in the latter group were slightly ill. Eight hours later the mice in the repeated group were treated again, and both they and those in the stoss group now looked identical. The repeated group were treated six times altogether at eight-hour intervals. In this experiment, except for the one early chance death, all animals in the treated groups survived during the 10-day observation period, and on this day they looked fit and there was no outward indication that they had been infected. In the control group several mice died between 10 and 18 hours after infection, and by the end of 24 hours 14 (28%) had died (Table I). Neither the immediate death in the stoss group (already mentioned) nor the death of a control mouse on the tenth day has been ascribed to pneumococcal infection in view of the negative smears and culture for pneumococci. The final mortality in the control group was 35 (70%).

TABLE I.—*Experiment 4. Length of Survival. Primary Infection*

Group	No. of Mice	Day of Death										Total Deaths
		1	2	3	4	5	6	7	8	9	10	
Stoss ..	49*											0
Repeated	50											0
Controls ..	50	14	13	7	1						1†	35 (70%)

Broth diluted 100 times. Dose contains 750,000 organisms.
* One sudden death immediately after infection. No cause at necropsy.
† No pneumococci grown from heart blood or peritoneal exudate.

All Experiments

Table II summarizes the results of primary infection in each experiment. In experiments 3, 5, 6, and 7 a greater number of mice died in the stoss group than in the repeated group, but the difference was small and was never sufficient to interfere with the completion of the experiment. Thus a reasonable and comparable number of mice from each treatment group were available for reinfection.

TABLE II.—*All Experiments. Mortality. Primary Infection*

Experiment	Group	Dose of Organisms	No. of Mice	No. Dying
1	Stoss	2,000	50	0
	Repeated	2,000	50	0
	Controls	2,000	50	17 (34%)
2	Stoss	150,000	50	0
	Repeated	150,000	50	0
	Controls	150,000	50	22 (44%)
3	Stoss	800,000	60	3 (5%)
	Repeated	800,000	60	0
	Controls	800,000	60	34 (57%)
4	Stoss	750,000	50	0
	Repeated	750,000	50	0
	Controls	750,000	50	35 (70%)
5	Stoss	690,000	50	5 (10%)
	Repeated	690,000	50	0
	Controls	690,000	50	50 (100%)
6	Stoss	830,000	50	2 (4%)
	Repeated	830,000	50	0
	Controls	830,000	50	50 (100%)
7	Stoss	830,000	50	14 (28%)
	Repeated	830,000	50	10 (20%)
	Controls	830,000	50	49 (98%)

Results: Reinfection

Experiment 4.—The results of reinfection in experiment 4 are shown in Table III. Two different reinfecting doses were used as in every other experiment except No. 1. It

TABLE III.—*Experiments 4a and 4b. Mortality and Length of Survival. Reinfection*

Group	No.	Day of Death 1	2	3	4	5	6	7	8	9	10	Total Deaths
Broth diluted twice. Dose contains $16·5 \times 10^8$ organisms												
Stoss	24	9	8	2								19 (79%)
Repeated	25	11	8	2	1							22 (88%)
Controls	25	8	7									25 (100%)
Broth diluted 10 times. Dose contains $3·3 \times 10^8$ organisms												
Stoss	25	3	6	2	0	1	1					13 (52%)
Repeated	25	4	11	3								18 (72%)
Controls	25	15	7	3								25 (100%)

was interesting that the difference in the size of the reinfecting dose was sufficient to reduce the mortality in the stoss group from 79% to 52%, and in the repeated group from 88% to 72%. The days on which the mice died are also shown.

Remaining Experiments

In all experiments except one the results differed in degree rather than pattern (Table IV).

TABLE IV.—*All Experiments. Results of Reinfection. Mortality*

Exp.	Group	Dose of Organisms	No. of Mice	Deaths	Percentage Mortality	Significance (P)*	Av. Survival Time (Days)
1a	Stoss	63×10^6	49	38	77	0·1–0·05	2·2
	Repeated	63×10^6	50	46	92		0·8
	Controls	63×10^6	50	50	100		0·2
2a	Stoss	3×10^6	25	13	52	0·2–0·1	5·8
	Repeated	3×10^6	25	19	76		3·2
	Controls	3×10^6	25	24	96		1·1
2b	Stoss	3×10^5	25	1	4		9·6
	Repeated	3×10^5	25	1	4		9·6
	Controls	3×10^5	25	19	76		3·3
3a	Stoss	6×10^5	27	13	48	0·1–0·05	5·8
	Repeated	6×10^5	29	6	21½		8·1
	Controls	6×10^5	30	27	90		2
3b	Stoss	6×10^4	27	3	11		9·1
	Repeated	6×10^4	29	3	10½		9·1
	Controls	6×10^4	30	18	60		4·6
4a	Stoss	$16·5 \times 10^6$	24	19	79		2·6
	Repeated	$16·5 \times 10^6$	25	22	88		1·9
	Controls	$16·5 \times 10^6$	25	25	100		0·3
4b	Stoss	$3·3 \times 10^6$	25	13	52	0·3–0·2	5·6
	Repeated	$3·3 \times 10^6$	25	18	72		3·5
	Controls	$3·3 \times 10^6$	25	25	100		0·5
5a	Stoss	31×10^4	21	6	29	0·01–0·001	7·3
	Repeated	31×10^4	25	18	72		3·4
	Controls	31×10^4	25	22	88		1·5
5b	Stoss	93×10^3	21	3	14	0·02–0·01	9·0
	Repeated	93×10^3	25	13	52		5·2
	Controls	93×10^3	25	18	72		0·9
6a	Stoss	167×10^3	24	3	12½	0·2	9·2
	Repeated	167×10^3	25	8	32		7·2
	Controls	167×10^3	25	25	100		0·9
6b	Stoss	5×10^3	24	5	21		8·5
	Repeated	5×10^3	25	6	24		7·9
	Controls	5×10^3	25	25	100		1·2
7a	Stoss	167×10^2	18	0	0		10
	Repeated	167×10^2	20	1	5		9·6
	Controls	167×10^2	25	24	96		2·1
7b	Stoss	5×10^3	18	0	0		10
	Repeated	5×10^3	20	1	5		9·6
	Controls	5×10^3	25	22	88		3·3
Total	Stoss		328	116	35·7	0·01–0·005	
	Repeated		348	162	47·6		
	Controls		360	322	89·4		

* Chi-square with Yates correction.

The mortality on reinfection of the treated groups showed a wide variation. In the stoss group the mean mortality was 35.7% (range 0 to 79%), in the repeated group it was 47.6% (range 4 to 92%), and in the control group it was 89.4% (range 60 to 100%).

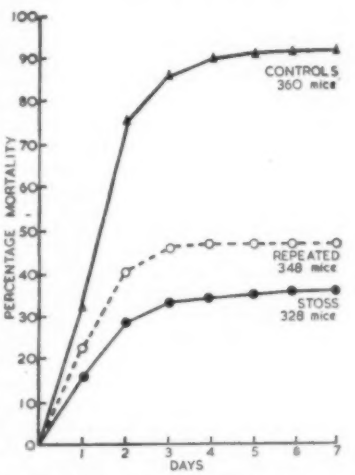
In experiments 5a and 5b the lower mortality in the stoss group was significant at the 1% level. In experiment 1a the difference was nearly significant at the 5% level in favour of the stoss group, and in experiment 3a at the same level in favour of the repeated group. In the remaining nine experiments any difference found might have been due to chance. However, in four of these the small differences which occurred were in favour of the stoss group; in the remaining five experiments the results were almost identical in the two groups.

TABLE V.—*All Experiments. Reinfection. Survival for 2 Days or Less Compared with Survival for more than 2 Days*

Exp.	Group	Total	Survived 2 Days or Less	Survived More than 2 Days	P*
1a	Stoss	49	38	11	0·1–0·05
	Repeated	50	46	4	
2a	Stoss	25	3	22	0·05–0·02
	Repeated	25	11	14	
2b	Stoss	25	1	24	
	Repeated	25	0	25	
3a	Stoss	27	10	17	0·3–0·2
	Repeated	29	6	23	
3b	Stoss	27	2	25	
	Repeated	29	3	26	
4a	Stoss	24	17	7	
	Repeated	25	19	6	
4b	Stoss	25	9	16	0·2–0·1
	Repeated	25	15	10	
5a	Stoss	21	6	15	0·01–0·001
	Repeated	25	17	8	
5b	Stoss	21	2	19	0·02–0·01
	Repeated	25	12	13	
6a	Stoss	24	2	22	
	Repeated	25	6	19	
6b	Stoss	24	3	21	
	Repeated	25	4	21	
7a	Stoss	18	0	18	
	Repeated	20	1	19	
7b	Stoss	18	0	18	
	Repeated	20	0	20	

* Chi-square with Yates correction.

Mortality within Two Days.—The number not surviving the first two days was compared with the number surviving more than two days (Table V). In experiments 5a and 5b the differences were great, and highly significant; in experiment 2a the difference was significant at less than 5%, and in experiment 1a almost at the 5% level. In the remaining experiments the differences were small.



Cumulative percentage mortality on reinfection. Difference between stoss and repeated groups significant ($0.01 > P > 0.005$).

Total Results.—The individual results of each experiment have been added together and are shown in Table IV. The mortality in the stoss group was 35.7% and in the repeated group 47.6%. The probability of this difference occurring by chance was less than 0.01. The cumulative percentage mortality is shown in the Chart.

Discussion

Reinfection

The results of reinfection are discussed first, since they form the main purpose of the investigation.

In general, fewer or the same number of mice died in the stoss group compared with the repeated group; the similar

mortality tended to occur when the reinfecting dose was lighter. There was, however, one exception to these general findings, and that was in experiment 3a, in which the repeated group showed a lower mortality than the stoss group when reinfected. The difference was not significant at the 5% level, and it occurred only once out of a total of 13 experiments.

It had been hoped at the onset that more clear-cut differences might have been obtained in each individual experiment, but the difficulties inherent in the nature of the experiment prevented this. The mouse is highly susceptible to pneumococcal infection, and therefore, under these conditions, mortality is a crude end-point. The success of each experiment depended not only on reinfection but on careful preliminary preparation by the primary infection together with its treatment. When immunity was sufficiently high, evaluation by mortality was not sensitive enough and would therefore not allow differentiation between the two treatment groups in every experiment. Finally it was not possible to handle more than 150 animals in each experiment; had larger numbers been used, greater differences might have been obtained. Nevertheless, in 10 out of 13 experiments, the mortality in the stoss group on reinfection was less than in the repeated group; in two of these ten experiments (5a and 5b) this difference was significant at the 1% level. It is unlikely that the lower figures for mortality in the stoss group in the remaining eight experiments were the result of chance, since in each experiment the trend was in the same direction. Moreover, when the results of all experiments were added together, the difference between survival in the two groups was significant at better than the 1% level in favour of stoss therapy (Table IV).

It is difficult to explain why those mice previously treated with a single dose should be more immune than those treated by multiple doses. A possible explanation might be that after the large single dose was no longer therapeutically active the damaged organisms and possibly "persisters" (Bigger, 1944a) which remained started dividing and again stimulated the response of the immune mechanism; the latter had already been stimulated when the animals were infected and treatment delayed for 10 hours, so that, although the time interval was very short, this was in the nature of a "booster" dose.

Size of Reinfecting Dose

It has been mentioned before that, except in experiment 1a, all reinfecting doses were of two strengths; this was done in order to increase the chances of discovering a difference in mortality. That this was of value was shown in experiments 2a, 3a, and 6a, in which the stronger dose revealed a difference in mortality which the weaker dose had failed to show.

Primary Infection

The results of primary infection revealed that in some of the experiments more mice in the stoss group died than in the repeated group; this was expected. It was, however, surprising that in three experiments (representing 150 mice) no deaths in the stoss group were recorded; this was achieved with only a single dose of chemotherapy, which had been delayed 10 hours after the onset of infection.

These low mortality rates might have been partly due to the contribution of the host. There is some evidence that this occurs in varying degrees. Thus Buck and Schnitzer (1945) showed that the combination of effective doses of antipneumococcal serum with subtherapeutic doses of penicillin exerted a striking synergic effect in mice infected with pneumococci. Rammelkamp and Kirby (1945) thought that the development of natural immunity was probably important in pneumococcal infection. Evidence in a negative sense was provided by Skinsnes and Woolridge (1948), who showed that protein depletion adversely affected the removal of pneumococci from the host's tissues. However, Florey (1952) has said that she does not consider that the natural antibacterial mechanisms can be taken into account in determining dosage of penicillin. It is known that specific defences are not necessary for some therapeutic successes with penicillin. For instance, Harrison (1946) abolished the immune response of highly immunized rabbits and mice with excess soluble antigen and showed that this abolition did not alter the effectiveness of penicillin. This might, however, have been due to the overwhelming effectiveness of the penicillin, and, had the dosage of that antibiotic been smaller, a difference might have been revealed.

Fate of Original Controls

The survivors of the primary infections in the control group were reinfected 10 days later at the same time as the other groups. This was done in order to compare the mortality of these original controls with that of the treated groups. It was possible to do this in only four of the experiments, as the mortality of the controls in the remainder was so high that either no mice or only a few were alive for reinfection. The fate of these controls is shown in Table VI.

TABLE VI.—*Fate of Original Controls*

Experiment	No.	Primary Infection Survivors	Deaths. Reinfection
1	50	33	18
2a	25	14	4
2b	25	14	0
3a	30	13	3
3b	30	13	0
4a	25	7	5
4b	25	7	3
Total ..	210	101	33

In experiments 1 to 4b about one-third (33 out of 101) of the survivors in the original control group died on reinfection. When the mortality figures for the stoss and repeated groups were calculated in the same experiments, it was found that 49% and 56.7% of the survivors died (Table VII). In these experiments there is a gradation in mortality when the latter is expressed as a percentage of survivors of the primary infection. Thus the most immune group were the original controls with a mortality of 33%, then the stoss group with 49% and the repeated group with 56.7%; and finally the new controls with a mortality of 90%.

TABLE VII.—*Fate of Survivors of Primary Infection on Reinfection*

	Survivors of Primary Infection	Deaths from Reinfection	Percentage Mortality
Original controls ..	101	33	33
Stoss	203	100	49
Repeated	208	118	56·7
New controls ..	210	188	90

The above figures suggest that the original controls—that is, those never treated—once they had survived the primary infection were much more immune (at the 1% level of significance) than either of those groups whose infection had been effectively treated before by chemotherapy.

The present findings in this respect may be similar to those reported by Pratt (1955) and by El-Rooby and Gohar (1956); these workers showed that, in treating typhoid fever with chloramphenicol, the earlier the treatment the higher the relapse rate. That delay in the treatment of pneumococcal infections with chemotherapy allowed a higher immunity to develop was well shown in Harrison's (1946) experiments in mice and rabbits. The longer treatment was delayed the greater the subsequent development of immunity, which was, however, accompanied by a greater immediate mortality.

In clinical practice, although the problem is twofold, attention is usually focused on only one aspect, the optimum treatment, and not on subsequent immunity. This is mainly because we are unaware of many of the factors causing recurrence of disease and uncertain of the part played by

chemotherapy in this respect. In a study of recurrences in pneumonia Strauss and Finland (1942) have shown that in those cases treated with sulphonamide there was a greater tendency for attacks to recur at shorter intervals, and for the same type of pneumococcus to occur more frequently in both attacks, than in those treated with serum or non-specific therapy. On the other hand, Jordan *et al.* (1950) have shown that, in any event, by the time the patient has symptoms the immune response has already been stimulated, and indeed that this response (measured by agglutination titres) was no different in those treated and those not treated by chemotherapy.

The present work in mice suggests that there is some difference in the degree of immunity developed, depending on the method of treatment when using the same drugs. Under the conditions of these experiments, the subsequent immunity was greater following stosstherapy than that following the repeated treatment.

Now that chemotherapy is so effective in the treatment of numerous infections, we should, I suggest, take into consideration the more remote and long-term factors as well as the immediate effect of treatment. In this way prevention as well as cure may be achieved.

Summary

As a result of the good response observed in children with acute respiratory infection when treated with a single dose of penicillin and sulphadimidine (stosstherapy), an experimental investigation into the relationship between method of treatment and subsequent immunity was planned.

The experiments were designed to investigate the immunity of mice which had been infected with virulent pneumococci and then treated with a mixture of sodium sulphadimidine and penicillin. There were two different treatment groups: (1) a single massive dose of sulphadimidine and penicillin (stosstherapy), and (2) six smaller doses repeated at intervals of eight hours. Treatment of both groups was delayed 10 hours after infection. Ten days later the survivors in each group were reinfected with challenging doses of pneumococci, and the immunity of each treatment group was evaluated by mortality.

In each experiment except one the single-dose group (stoss) showed either a lower or a similar mortality on reinfection compared with the group having repeated doses. When all the results were taken together, a significant difference at the 1% level in favour of stosstherapy was observed.

So far as these results can be applied to natural human infection, the greater immunity of the stoss-treated group over the repeated-dosage group offers a further reason for using stosstherapy in suitable cases of human pneumococcal infection.

I thank Miss M. Mann for technical help and for her care of the animals; Dr. C. Mackenzie for help with the experiments; the pharamaceutical department for preparing the small doses of penicillin and sulphadimidine; and Dr. P. R. Evans, Professor R. Knox, and Dr. P. E. Polani for their criticism of the manuscript.

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SPLENIC ARTERIAL ANEURYSM

BY

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Aneurysm of the splenic artery was mentioned by Beaussier in 1770. Winckler (1905) recognized the condition in the living, Högler (1920) made the diagnosis before operation, and Lindboe (1932) was the first to make a radiological diagnosis. Perhaps the most famous example was that of President Garfield, who died from a ruptured traumatic aneurysm of the splenic artery two months after being shot by an assassin.

Splenic arterial aneurysm is a rare condition, and rupture is usually fatal. Owens and Coffey (1953) reviewed 204 fully documented cases, and Hill and Inglis (1955) found 35 survivors after surgery, including only nine after rupture. A further four recoveries after rupture have been reported by Gallagher and Hudson (1954), Parrella (1955), Colangelo (1955), and Owen, Holmes, and Scannell (1957). Among these 13 survivors after rupture were four pregnant women (Owen *et al.*, 1957).

Diagnosis before rupture is uncommon (Hughes and Joske, 1955; Riemenschneider, 1955). Berger, Forsee, and Furst (1953) considered their case to be the eleventh diagnosed before operation in the English literature.

There are many unrecorded cases of splenic arterial aneurysm, particularly those seen at necropsy, and those diagnosed radiologically and not confirmed by operation.

The purpose of this paper is to discuss five patients with splenic arterial aneurysms operated on in Mansfield during the past two years. Four of the five survived. In two the aneurysm had ruptured; one, a pregnant women with a porto-caval shunt, recovered. The other three were diagnosed on radiological grounds before operation. In two the operative removal was incidental to that of a carcinoma—of the oesophagus in one, and of the kidney in the other. The remaining patient had urological symptoms and hypertension, but none referable to the region of the aneurysm.

Case 1. Staged Rupture—Splenectomy—Death in Anuria

A publican of 42 was admitted as an emergency case with pain in the left hypochondrium. A severe attack of pain in the left loin passing to the left chest in the mid-axillary line,

had occurred four days previously, but cleared up with rest in bed. He started work three hours before admission. There was a sudden very severe pain in the left hypochondrium; he became grey, sweating, and collapsed, but again improved.

He collapsed again soon after admission, and was thought to have had a coronary thrombosis or possibly an acute pancreatitis. He was pulseless and cyanosed, with epigastric and left-sided pain and tenderness. An electrocardiogram was normal, as were the urinary diastase and a plain radiograph of his abdomen taken as he began to improve. Next day his general condition was better and the pain was less, but it still occurred in spasms. The blood pressure was 130/80; the abdomen moved well on respiration, but there was general tenderness, with dullness in the flanks. His haemoglobin was only 52%. A diagnosis of intraperitoneal bleeding was made.

At operation (Mr. P. A. Read) the abdomen was full of blood and clots, with old clots in the lesser sac, into which the splenic aneurysm near the pedicle must have ruptured. Splenectomy was performed with excision of the aneurysm, and 2 litres of blood was transfused.

Although his immediate post-operative course was satisfactory, he became anuric, and died three days after operation.

Necropsy revealed extensive hypostatic pneumonitis, parenchymatous degeneration of liver, kidney, and brain, and toxic petechiae on several surfaces.

Case 2. Ruptured Splenic Aneurysm in Pregnancy after Porto-caval Shunt—Splenectomy—Recovery

A housewife of 36 was admitted as an emergency case with gross intraperitoneal bleeding on December 24, 1956. She was known to have had an enlarged spleen since the age of 20, and Dr. R. J. Twort had confirmed that she had portal hypertension after a haematemesis in 1953. A splenic venogram showed an intrahepatic block. Liver-function tests were normal. In the summer of 1956 Mr. T. B. Field carried out an end-to-side porto-caval shunt. There was fine multilobular cirrhosis of the liver. The liver and spleen reached to the level of the umbilicus.

It then became apparent that she was in her third pregnancy. This was proceeding uneventfully, and she attended the antenatal clinic in early December. On Christmas Eve, in the 26th week of pregnancy, while doing the Christmas decorations, she had a sudden severe pain in the left side of the epigastrium passing to the right side, and she fainted. Dr. M. E. O'Sullivan diagnosed gross intraperitoneal haemorrhage from the spleen, and noted that her previously easily palpable spleen could only be felt on "dipping." Mr. S. C. Anderson and the flying squad were summoned urgently, and 1 litre of blood was transfused without preliminaries. Fortunately, her blood group was known, and this prompt action enabled her to reach King's Mill Hospital alive.

At operation some four hours after her initial symptoms, some 3 litres of blood was sucked out of the peritoneum as well as clots. A bleeding aneurysm was found near the hilum of the spleen, and a splenectomy was performed with excision of the aneurysm. There had been considerable bleeding behind the peritoneum and into the mesentery. Her condition was critical during the operation, and a further 2 litres of blood was transfused by two drips. This operation was done under general anaesthesia, given by Dr. McNab.

Specimen.—Dr. A. B. Hill reported that this showed a venous aneurysmal sac and two adjacent arterial aneurysmal sacs 4.4 by 4.2 and 2.2 by 3 cm. in the main trunk near the hilum. Both showed intimal degeneration, fragmentation, atherosclerosis, and patchy calcification. The larger sac showed an area of progressive thinning down to a focus of 0.3 cm. diameter—a mural rupture. The specimen was radiographed, though it is unlikely that the degree of calcification would be recorded on a routine radiograph. The spleen showed reticular hyperplasia, and portal hypertension was suggested. There was no extrasplenic arteriovenous communication.

Progress.—The patient aborted on the second post-operative day. Later she had rigors and chest pains, and was considered to have had recurrent pulmonary infarcts associated with a *Streptococcus pyogenes* septicaemia. Dilatation and currettage was done for septic retained products by Mr. S. C. Anderson two weeks after operation. She was treated with penicillin and streptomycin, and later with erythromycin. She made a slow recovery, with a relapse of the septicaemia, again requiring erythromycin. She was well when seen fifteen months after operation.

Case 3. Splenic Aneurysm and Left Renal Adenocarcinoma—Splenectomy and Nephrectomy—Recovery

A housewife of 63 was referred with a history of left renal colic and haematuria for two weeks. There had been occasional pains in the left loin for three years. Physical examination was not informative. An intravenous urogram showed a filling defect in the left kidney and a calcified splenic aneurysm. Retrograde pyelography (Fig. 1) confirmed a space-occupying lesion in the kidney and also in the pelvis—possibly blood clot.

FIG. 1.—Case 3. Ascending urogram showing filling defect due to adenocarcinoma of kidney and calcified splenic aneurysm.

The kidney and spleen were excised through the bed of the eleventh rib, and recovery was uneventful. She was well when seen a year after operation.

Specimen.—The kidney showed a typical adenocarcinoma. There was a calcified aneurysm of the main splenic artery near its division measuring 3.3 by 1.5 cm. (Fig 2A).

Case 4. Splenic Aneurysms and Carcinoma of the Oesophagus—Block Resection—Recovery

A housewife of 75 was referred by Dr. J. C. Pease with dysphagia from a carcinoma of the lower oesophagus. She also had three calcified splenic aneurysms (Fig. 3). She had had a partial gastrectomy 20 years before by Mr. E. A. Nicoll for gastric ulcer.

Through the bed of the ninth rib a resection of the lower oesophagus, spleen, part of the pancreas, and remnant of the stomach was done, with a Roux loop oesophagojejunostomy. She was well when seen a year after operation.

Specimen.—The largest of the three calcified splenic aneurysms at the division of the splenic artery measured 2.9 by 1.8 cm. (Fig. 2C).

Case 5. Splenic Aneurysm and Pyelitis—Splenectomy—Recovery

A housewife of 57 was known to be hypertensive and overweight. She had had a partial thyroidectomy for toxic goitre four years previously. She now had what seemed to be a typical attack of pyelocystitis, due to *Escherichia coli*. There was some haematuria. An intravenous urogram showed normal upper urinary tracts and a calcified splenic aneurysm (Fig. 4). There was no other abnormality. The blood pressure was 190/110. The urinary symptoms responded to nitrofurantoin, to which drug the organisms were sensitive.

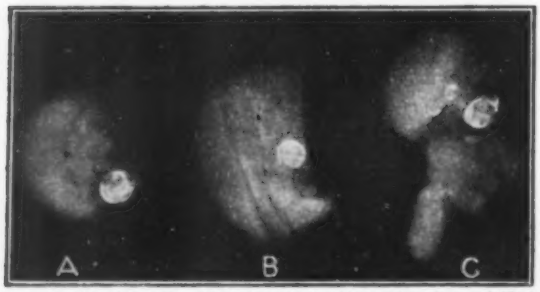

FIG. 2.—Radiographs of the excised spleens showing calcified aneurysm. A=Case 3. B=Case 5. C=Case 4 (the specimen also includes some stomach, oesophagus, and pancreas).

FIG. 3.—Case 4. Plain radiograph showing three calcified splenic aneurysms.

The spleen and the aneurysm were excised. Recovery was uneventful. She was well when seen a year after the operation.

Specimen.—The calcified aneurysm measured 2.6 by 2.1 cm., and was situated near the branching of the main trunk of the splenic artery (Fig. 2B).

Discussion

The features of this condition are well described elsewhere (Sherlock and Learmonth, 1942; Chalmers, 1949; Owens and Coffey, 1953; and others), and mention is here made only of the salient points.

Incidence

Owens and Coffey (1953) found 37 splenic aneurysms in 96,471 necropsies, an incidence of 38 in 100,000. It is the most common intra-abdominal aneurysm after that of the aorta. While other aneurysms are five times more common in men, splenic aneurysms occur twice as often in younger women as in men. The average age of identification is 48, and, in round figures, half the women are of childbearing age, and half of these are pregnant.

All radiologists of experience have seen numbers of these calcified aneurysms, but I have not been able to find any large series or collected radiological statistics.

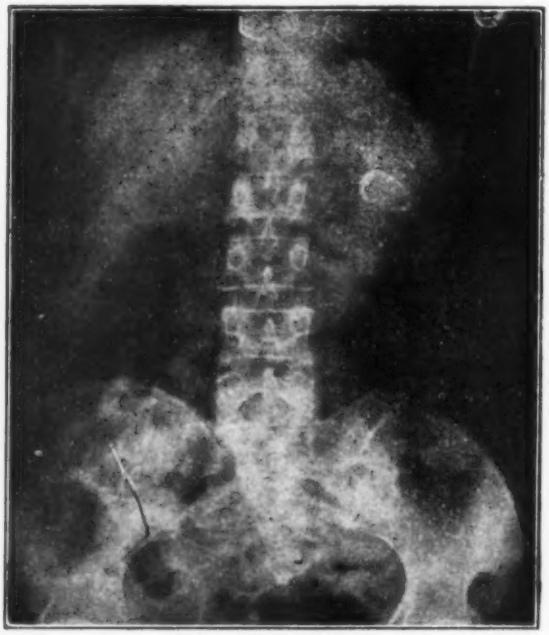

FIG. 4.—Case 5. Plain radiograph showing calcified splenic aneurysm.

Pathology

The commonest pathogenetic factor is arteriosclerosis, then embolic phenomena, portal hypertension, congenital causes, trauma, and infection in that order of frequency.

Splenomegaly occurs in 45% of cases, and portal hypertension, as in Case 2, in half of these. Rupture in pregnancy occurs after the sixth month; in a third of these there is no obvious cause. In some patients rupture of the splenic artery occurs without a definite aneurysm. This was the case in three of the four previous recoveries after rupture in pregnancy, all these patients being women in their early twenties.

The aneurysm is single in some three-quarters of the patients, and in three-quarters the main trunk of the splenic artery is involved. The average diameter of the aneurysms is 3.1 cm.

Ruptures most commonly occur into the peritoneum, sometimes into the lesser sac or retroperitoneally, and occasionally into the stomach, colon, mesentery, and even into the chest.

Clinical Manifestation and Diagnosis

The aneurysm may be an incidental finding, diagnosed by the characteristic roughly circular calcified shadow, often with a loss of continuity where the sac communicates with the artery, and with central stippling, as in Cases 3, 4, and 5. In these patients the position of the calcified aneurysm varied from opposite the eleventh dorsal to opposite the second lumbar vertebra. A host of symptoms, many referred to the gastro-intestinal tract, may be ascribed to the aneurysm, and unrelated urological symptoms may be present, as in Cases 4 and 5, and require radiography.

The usual symptom before rupture is pain in the abdomen, particularly in the left upper quadrant, sometimes radiating to the back, the chest, and the left shoulder. Between attacks the patient is often well. Some of these attacks of pain are probably small leaks, and there may be a "staged" rupture as in Case 1. Haemorrhage may be precipitated by trauma or exertion: the weekly wash, a fit of laughter, opening the bowels, dusting a picture on Christmas Day, and sexual intercourse have all preceded rupture in reported cases. A warning haemorrhage may precede catastrophic bleeding, which generally occurs within 48 hours, but there may be no symptoms before rupture, as in Case 2. A bruit was heard in 9%, and a pulsatile tumour was felt in 8% of the reported cases; but, unfortunately,

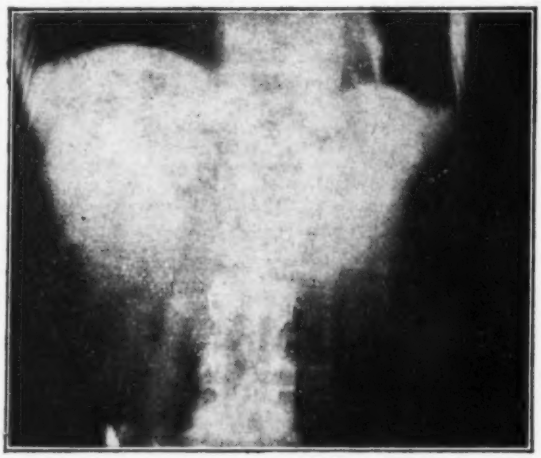

FIG. 5.—Tomogram showing calcified shadow misdiagnosed as splenic aneurysm.

these almost pathognomonic signs are infrequent, and were absent in the five cases here reported.

Haematemesis and melaena may follow rupture into the stomach or intestine, and, while Owens and Coffey (1953) state that as many as 30% of patients have these complications, the picture is usually that of frank internal haemorrhage. Often the bleeding is at first retroperitoneal, and this was the case in the only other patient with a ruptured splenic aneurysm that I have seen. I transfused this African patient in a military hospital, but he soon died with massive bleeding.

Before rupture, aortography has been used as an aid to diagnosis (Riemenschneider, 1955; and others). It might be considered meddlesome if a confident diagnosis had been made, but it may differentiate a splenic aneurysm from a calcified echinococcal or splenic cyst, a calcified tuberculous node, or other shadows. Calcification of a tortuous splenic artery, without aneurysm, may also cause confusion without aortography. A confident radiological diagnosis of splenic aneurysm was made in an elderly lady who presented with haematuria, due to a papilloma of the bladder, and a right inguinal hernia. Cystodiathermy, repair of her hernia, and a laparotomy were done. The cause of the calcification was not found in spite of splenectomy and resection of the whole splenic artery. Fortunately she is none the worse. An aortogram has not been done, and presumably the calcification is still in the body of the pancreas (Fig. 5).

When there are symptoms, confusion with coronary disease and pancreatitis is common. Pancreatitis may also be present, with raised pancreatic enzymes in the blood and urine (Colangelo, 1955; Hughes and Joske, 1955).

In pregnancy, concealed accidental haemorrhage is the usual differential diagnosis, but ruptured splenic aneurysm must be borne in mind. Dr. M. E. O'Sullivan, who called the flying squad in to Case 2, had seen the young wife of a fellow British officer in Malaya die after an operation for a ruptured splenic aneurysm in pregnancy.

Treatment

Resection of the artery and splenectomy form the treatment of choice. Double ligation of the artery or resection of the sac has been successful in four cases. Many calcified aneurysms have been treated conservatively, apparently without disaster.

Owens and Coffey (1953), in their authoritative review, state: "At the risk of belabouring the obvious, it may be categorically stated that the treatment of an aneurysm of the splenic artery is exclusively surgical. Once a diagnosis of this lesion is made, or strongly suspected, prompt operative interference is essential." Most others endorse this view, and advocate prompt surgery, whether symptoms are present or not. There are indeed still only a dozen survivors reported after rupture.

Lennie and Sheehan (1942) recommend caesarean section in rupture in pregnancy, while Gallagher and Hudson (1954) advise against emptying the uterus, which seems more reasonable. In one report a patient died during the caesarean section undertaken to facilitate the search for the bleeding-point.

Ronnen (1953), from the Hague, advises observation provided the aneurysm is "the size of a cherry or smaller," completely calcified except where it joins the main trunk, asymptomatic, and not in a woman of child-bearing age or in a patient with hypertension. According to these criteria, Case 3 would be on the borderline, with an almost completely calcified aneurysm the size of a cherry, but operation was needed in this case for the renal carcinoma, and splenectomy was easily done at the same time. Case 4 merited operation because of the size of one of the aneurysms, quite apart from the carcinoma of the oesophagus, and Case 5 because of the hypertension. Ironically, Ronnen would have advised against operation in the case, mentioned above, of the smaller "splenic aneurysm" diagnosed confidently by radiology but not confirmed at laparotomy.

A good case can be made for conservatism in the elderly or when the patient is a poor operative risk.

Ronnen (1953) states that he could find no case of a ruptured calcified splenic aneurysm in the literature. This is an important point. Some incompletely calcified splenic aneurysms rupture (Tagart, 1952), but often the question of calcification is not specifically mentioned in reports, nor are *x*-ray films always taken before operation, or of the specimen after operation, or at necropsies, in cases of rupture. Complete calcification can be demonstrated only by detailed anatomical study. Berger *et al.* (1953), from a study of the literature, state that 35% of splenic arterial aneurysms rupture. It is difficult to assess the number of aneurysms at risk, and also the number that rupture, but this figure seems far too high.

However, until the danger of rupture can be foretold with accuracy, it would be wise to treat all splenic arterial aneurysms with great respect, and, as a general rule, to excise them.

Summary

Five cases of operative removal of splenic aneurysms are reported. In this series there was one death following rupture of an aneurysm, and one recovery after rupture of an aneurysm in a pregnant woman; another patient had a porto-caval shunt. In the three patients with unruptured aneurysms the diagnosis was made by the radiologist before operation, and these patients survived.

I am indebted to Dr. A. B. Hill for the pathology reports; to Dr. E. J. S. Townsend for the radiographs; to Dr. A. Hegarty, who anaesthetized four of these patients; and to my surgical colleagues, Mr. F. J. Milward, under whose care Case 1 was admitted, and Mr. A. McEwan Smith, who referred Case 5.

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CLINICAL TRIAL OF ACEPROMAZINE MALEATE IN CHRONIC SCHIZOPHRENIA

BY

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A new derivative of the phenothiazone group of tranquillizers, acepromazine maleate ("notensil"), was first given a clinical trial in France by Delay and Pichot (1957), who studied its effect in 11 psychoneurotic outpatients and 20 severe psychotics. The use of acepromazine in other kinds of disorders has already been mentioned by Stafford-Clark (1957), and it was understood that our project was only part of the trials planned in this country into the use of acepromazine in different clinical conditions. The largest single clinical group of diseases with behaviour disturbance in a mental hospital remains schizophrenia, and we decided to limit our study to this disease. Our aims were (1) to ascertain whether treatment with acepromazine is of value in chronic schizophrenic patients with behaviour disorders, and (2) to record the incidence of side-effects and toxic effects.

Methods

We defined chronic schizophrenia as an illness characterized by a disorder of emotion and thought, hallucinations, and behaviour disturbances of more than one year's duration. The patients selected numbered 86—42 in the treatment group and 44 as controls. For various reasons four patients in each group were withdrawn. All had been known to us for at least one year and the diagnosis was agreed upon. Patients with a history of jaundice or evidence of active peptic ulceration were excluded.

Before starting the trial our colleagues agreed to discontinue the use of tranquillizers on schizophrenic patients so that we might observe whether, on withdrawal of these drugs, the patients remained in remission or showed signs of relapse. Those who relapsed were then considered for inclusion in this trial, and if accepted, their clinical, nursing, and psychometric ratings were carried out. Clinical rating was made by one of us (J. F. C.) on the basis of a scale described by Boardman *et al.* (1956), whilst the nursing staff used the rating scale of Baker and Thorpe (1956). Psychometric assessment with a group of tests designed for psychotic behaviour was attempted, but it has not been possible to include these findings in our paper.

Patients were chosen from any ward in the hospital and allocated to treatment or control groups on the basis of Bradford Hill's (1955) prescribed random order chart. This chart was held by the chief pharmacist, who supplied the appropriate substances in identical containers.

The drug, or placebo, was given orally in tablet form at an initial dosage of 50 mg. three times a day. This was increased by 50 mg. a day until a daily total of 300 mg. (given in three equal doses) was reached on the fourth day. We aimed to maintain the dosage at this level for six weeks, although some modifications had to be made when side-effects were encountered. Only those patients who completed a full course of treatment were included in our series.

The clinical and nursing ratings were carried out at weekly intervals during the six weeks of treatment. At the end of this period an approximate clinical assessment of the efficacy of the treatment was made by classification of the subjects into the following groups: (1) improved (to cover all variations between number and severity of symptoms materially less up to a complete remission); (2) not improved; and (3) worse (symptoms aggravated and behaviour more disturbed).

A further statistical assessment of the changes in clinical and behaviour rating scales was made by means of a test on the differences in the ratings before and after treatment.

Distribution of Clinical Types and Comparison of Groups

The 78 patients taking part in the trial were classified according to clinical groups (Table I).

TABLE I

	Control Group	Treatment Group	Total
Simple	11	11	22
Paranoid	10	11	21
Catatonic ..	13	10	23
Mixed	5	6	11
Hebephrenic ..	1	—	1
Total ..	40	38	78
Males	19	20	39
Females	21	18	39

The average age and duration of stay in hospital for each group are shown in Table II.

TABLE II

	Control Group	Treatment Group
Age	44·32 years	48·18 years
Duration of stay	13·29 ,,	13·25 ,,

As all our subjects had been in hospital for over a year it followed that many of them had previously received some kind of physical treatment. The two groups are compared

in Table III. It is not possible to say whether any of the differences are significant, as the groups are too small for comparison statistically.

TABLE III

Group	E.C.T.	Coma Insulin Treatment	Leptazol	Leucotomy	Tranquillizers	Lithium
Control ..	25	3	1	8	20	2
Treatment	25	2	3	4	4	—

A check was carried out on the distribution of patients ward by ward; this is too parochial to enumerate, but it was established that there were no significant weightings.

Toxic Effects and Side-effects

We did not observe Parkinsonism, jaundice, or dermatitis, but were seriously troubled by the incidence of hypotensive reactions in the treatment group. Of the 42 patients in the treatment group, four (three females and one male) had such severe hypotensive reactions that treatment was discontinued. The fall of blood pressure was considerable even on as small a dose of acepromazine as 10 mg., and in the male patient was associated with a major epileptic fit and depression of corneal reflexes. Of the 44 in the control group, three refused to take tablets and one collapsed as though hypotensive, but there was no loss of consciousness and the blood pressure was not depressed. In these four patients, also, treatment was discontinued.

Clinical Changes

The effects observed, using the criteria mentioned above, are shown in Table IV. An examination of the scales of behaviour and symptom rating showed that an analysis of

TABLE IV

	Treatment Group	Control Group
Worse	5	5
No change	24	34
Improved	9	1

variance represented the most satisfactory method of assessing whether the changes were significant statistically. With this method, allowance was made for the variation between patients. The figures of the summary of the analysis of variance are included in the Appendix.

The assessment showed that with this method there was no significant change in the nurses' rating of behaviour following acepromazine maleate therapy. The clinical rating by the doctor was dealt with in a like manner, and, although this showed that there was some improvement, it did not reach a high level of significance. As described above, a subjective assessment of clinical change was made. To obtain 9 cases of improvement among 38 treated and only 1 case of improvement among 40 not treated is highly significant ($P=0.00556$) (Fisher's exact test).

Discussion

In a study by Wing (1956), the degree of control of the environment has been increased by siting all of the subjects in what is virtually a research ward. We have tackled the problem in a different way by arranging that our patients came from any ward. Thus any environmental weightings were distributed throughout both treatment and control groups, and weighting by individual environmental factors was less likely. Although any purposeful form of activity in mental hospital wards can be of great value, there was no evidence that the special attention given to all of the patients resulted in improvement in the control group.

A direct interpretation of our results has been found difficult, particularly because we have been advised not to attach too much importance statistically to the findings under "subjective clinical assessment." This leaves us, therefore, to consider the results of changes in both the nurses' and the doctors' ratings. In neither of these was there any evidence of highly significant change, and this finding fits in with our working clinical impression that under the conditions used in this investigation the drug did not produce a dramatic response. It is perhaps important to observe that no worsening of behaviour occurred in our treatment group (the means of the nurses' rating in the first and last weeks are 12.4 and 10.87). The disparity of our findings with those of Delay and Pichot is probably accounted for by the different type of clinical material, although, in view of the recent comments on the use of tranquillizers in schizophrenia, variations in dosage can influence results.

In the Maudsley Bequest Lectures (R.M.P.A., 1957) two methods of administration were put forward. Either the "low-dose" method, in which the drug is given in a dosage of up to 600–800 mg. daily for a period of three to four months, or the "high-dose" method, in which the dosage of up to 2–3 g. is given for only 7 to 14 days. We suggest that, if further investigations with acepromazine are contemplated, either the low-dose method should be continued for a much longer period of time or the high-dose technique should be applied. The French workers used parenteral injections, and, while this method of administration is desirable for uncooperative patients, it is not likely to influence the efficacy of the drug. Fluid medicine for oral use is desirable for psychotic patients where co-operation may be limited, and our study could perhaps be extended on these lines.

Rosenheim (1957) has commented on the problem introduced into any investigation of a drug known to have side-effects or toxic effects. An additional problem for the psychiatrist is that an objective assessment of psychiatric symptoms and signs is fraught with difficulties, and Wing (1956) commented on this and felt that her findings should be interpreted with caution. In our trial we found a new complication arising in that some of the nursing staff regarded the medicine being given to each patient as a challenge to them to find out whether the patient was having the placebo or not. We noticed that this curiosity extended even to the nurses tasting the tablets, and as there was a difference in taste between the placebo and drug it may have influenced their assessment of behaviour. We do not know if this observation has been made before in a clinical trial, but certainly more attention should be paid to the standard of placebos, particularly if the trial is to be "controlled" and statistically assessed. It is impossible to say how much this has influenced our findings, but in designing any controlled investigation we believe it important that this factor should be taken into account.

The occurrence of hypotensive side-reactions in 4 of the 42 patients in the treatment group was most disturbing, particularly as in one of them the changes were observed even on reducing the dosage to 10 mg. The sequence of clinical events in these cases was so dramatic that it could be argued that the observer recognized that the patient was in the treatment group and thus subsequent ratings might have been biased. We did not take this view, although it became necessary for three out of these four to be excluded from the trial as an adequate dosage of acepromazine could not be maintained on account of the hypotensive reaction. In one of our male patients receiving acepromazine the hypotension was associated with a drowsy state of consciousness, in which the corneal and limb reflexes were disturbed. The occurrence subsequently of an epileptic fit suggested that these changes in the reflexes may have been associated with a post-ictal state. It seems, however, that acepromazine, like promazine and chlorpromazine, is able to potentiate epilepsy.

We believe that the findings of our study justify the value of the preliminary trial of a drug before the manufacturers embark upon wholesale advertising and distribution. That

our study concerned only a limited type of schizophrenic illness must be borne in mind when considering its significance.

Summary

A clinical trial is described in the use of acepromazine maleate (notensil) in chronic schizophrenia.

The drug has a limited value.

Side-effects (hypotension and epilepsy) were observed.

The difficulties of making this kind of trial objective are described. The importance of the standard of the placebo is stressed.

We are grateful to Messrs. Bengers for supplying notensil tablets and placebo and for help with the statistical and secretarial facilities. We are grateful also to Mr. R. Bevan, senior psychologist, Hellingly Hospital, and to Mr. P. Slater, of the statistical department of the Institute of Psychiatry, for carrying out a statistical assessment and giving us advice on these matters. In the clinical field we are indebted to many of the staff of Hellingly Hospital, and particularly to our medical superintendent, Dr. David Rice, for having made this study possible.

APPENDIX

Summary of Analysis of Variance (Doctors' Rating Scale—Symptoms)

Source of Variance	Sum of Squares	D.F.	Mean Square Variance
Total variance	1,173·47	151	
Between persons	766·97		
,, treatments (treatment/control)	7·17	1	
,, sexes	24·17	1	
Sex/treatment interaction	43·00	1	
Residual variance between subjects	692·63		
Variance between trials (first/final)	35·06	1	
Treatment/trial interaction	17·11	1	17·11
Sex/trial interaction	2·95	1	
Sex/treatment/trial interaction	0·90	1	
Residual error	350·48	72	4·868

$F = \frac{17·11}{4·868} = 3·515$. $0·10 > P > 0·05$ on a two-tailed test.

The difference is in the expected direction, that of improvement, but it does not reach a high level of significance.

Summary of Analysis of Variance (Nurses' Rating Scale—Behaviour)

Source of Variance	Sum of Squares	D.F.	Mean Square Variance
Total variance	2,225·26	151	
Between persons	1,831·26		
,, sexes	182·48	1	
,, treatments	0·94	1	
Sex/treatment interaction	4·95	1	
Residual variance between subjects	1,459·47	72	
Variance between trials	46·42	1	
Treatment/trial interaction	6·74	1	6·74
Sex/trial interaction	1·02	1	
Sex/trial/treatment interaction	0·21	1	
Residual error	339·61	72	4·717

$F = \frac{6·74}{4·717} = 1·429$ (non-significant).

The assessment showed that, using this method, there was no significant change in the nurses' rating of behaviour following acepromazine therapy.

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DISTURBED RELAXATION OF LIMBS

BY

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In a few individuals relaxation of limbs in the sitting or recumbent positions, or during sleep, is repeatedly interrupted by a train of motor and sensory disturbances. Though the legs are chiefly affected, occasionally the arms also participate in this disorder. These phenomena can be promptly abolished by suspending relaxation and engaging the affected limbs in active movements, and this latter feature constitutes the chief diagnostic touchstone. According to the nature of the main symptom engendered by relaxation, several groups can be recognized, but certain general features apply to most cases.

General Features

After its onset in early adult life, the disorder persists for many years, during which it remains subject to marked fluctuations without ostensible cause. While the distribution is usually bilateral, occasionally only one limb may be affected. Typically the symptoms supervene after relaxing in an easy-chair in the evenings, when travelling, at the theatre or cinema, or when reading or watching television. The symptoms constantly reappear after a period of untrammelled relaxation of the limbs, a period which varies according to the severity of the case. Only by assuming the erect position or by walking can these symptoms be made to disappear completely for a time. The malady shows a pronounced heredo-familial incidence in an appreciable proportion of cases. Pregnancy and anaemia tend to exert a strong aggravating influence. If the testimony of the patient's spouse is available one often learns that some twitching and jerking of the legs occurs during sleep. This can be of such frequency and severity as to be very disturbing to the other occupant of the double bed.

Cases fall into the following groups according to the nature of the main symptoms: myoclonus, pain and myoclonus, pain, "sleep-pain," and "restless legs."

Myoclonus Group

A sudden, quick, localized muscle contraction, with or without a movement of the limb, occurs in the legs under the provocative conditions mentioned. The myoclonus is apt to recur in the same situation again and again until the sequence is broken by activity, yet on another occasion a totally different group of muscles may be affected in a similar manner.

Case 1.—A woman aged 39 had for the past 11 years, after relaxing in an easy-chair in the evenings, been subject to sudden recurring muscle twitches, mainly in the left leg—"even in the middle of reading an absorbing book or watching the Mount Everest film." These muscle contractions, which may affect any muscle group of the legs, could be felt and seen; though powerful, they only rarely caused movements of the limbs. Occasionally the resulting jumping of the limb resembled a "knee-jerk." This disorder affected her particularly in bed when about to go off to sleep. Though the jerking "banished sleep," it nevertheless continued to recur at short intervals. She had to remain standing for at least 15 minutes to break the sequence. A shorter period would not suffice, since on returning to bed the muscle twitching reappeared almost at once. She learned to recognize a "non-relaxed sensation"

in the inner groin as a prelude to and concomitant of the myoclonus. While this sensation endured, any handling or touching of the affected limb was apt to "send up a sensation in the groin and might be followed by a jerk." Occasionally myoclonus in her sleep caused her to awaken. Her brother was similarly affected, and often "had to watch television standing up." Her father used to say: "I can't keep my legs still." She recalled that her mother "used to have bad nights because dad could not keep still."

Case 2.—A woman aged 28 said she had "involuntary jumpiness when I sit down and relax." Her legs were affected more than her arms. "My husband says that I am jumping all night in my sleep." A few slight episodes occurred during the past five years, but myoclonus became of disabling degree during her two pregnancies. She was "in an exhausted state at nights" during the first pregnancy, since myoclonus interfered with sleep. "I should imagine if you get it badly you'd commit suicide."

Case 3.—This patient, a woman aged 70, said that, for the past 40 years, if she didn't do anything and sat in the chair or lay down "my legs keep jumping—I must then get up." For the past six months she had similar "jumping" in the arms. Myoclonus became such a hindrance to sleep five years ago that she was given morphine. "If I were to leave off tablets I would get no rest at all."

Case 4.—A man aged 48 said, "After resting I feel as if I am a syringe, and I am sucking up something from the bottom of the legs; this makes my legs kick." Unless he got up and walked about, the myoclonus recurred in precisely the same manner every 30 seconds. Of necessity this interfered with his sleep, and he had to give up driving because, as a consequence of lack of sleep at night, he became liable to fall off to sleep while driving. His mother was probably similarly affected.

Pain and Myoclonus Group

After an adequate period of relaxation of the limbs, pains appear which are described variously as "aching like toothache," "gnawing pain," and "throbbing pain." The pain rapidly mounts in severity and culminates in a myoclonic twitch.

Case 5.—A man aged 77 said that within half an hour of sitting or lying down he experienced a sensation in the region of the right ankle "like a dog gnawing." This sensation heralded the onset of paroxysmal pain—"stabbing"—in the lower part of the right leg. According to him, this "stabbing" caused the leg to kick out. As soon as the "gnawing" sensation appeared he tried to avert the "stabbing" by walking about or, if this was not possible, by standing up and marking time. These disturbances prevented him from obtaining rest and sleep for more than short periods. For many years he received treatment for a minor degree of arthritis of the right ankle. He had been referred to the neurosurgical centre for the purpose of leucotomy, since he had expressed suicidal intentions. Five months later he was readmitted to the centre following a severe head injury. Despite his age he made a complete recovery, and when seen six months after the accident he stated that the right leg had continued to trouble him seriously until the date of the accident. Since then the right leg had been entirely free from the pain, but recently somewhat similar pains, but of lesser severity, had occurred in the left leg. One daughter was reported to be suffering from similar disturbances of her legs when resting.

Case 6.—A woman aged 44 said: "For some years, directly I sit down and relax I get neuralgia pain in the right leg below the knee; the pain gets to a pitch and then makes the leg jump; the pain and jumping continue until I start moving about, and this relieves them."

Case 7.—A woman aged 63 for many years had "a fidgety, nervy feeling" in her calves after sitting for more than three hours, or during a long train journey. "It would stop if I walked across the room." Recently these symptoms appeared more readily, and were much more intense—"as if something tearing the calves." "If I don't get up and walk, legs jump of their own accord—walking is the only thing that stops it. Massaging the legs is of no help, but a hot bath may relieve it. I call it torture—though it does not make me feel ill it spoils all my pleasure." She had been told that jerking of the legs continues in her sleep. "I always wake up with the fidgety feeling in the legs." One sister and two nieces were similarly affected. Following medication with phenobarbitone she improved considerably, but relapsed for no apparent reason. Examination revealed anaemia of moderate severity—haemoglobin 67%, colour index 0.66. Injections of "imferon" produced a dramatic relief of her symptoms.

Case 8.—This patient, aged 39, had had four pregnancies during the past 14 years. During each of them the following symptoms occurred, causing her much distress, mainly because of interference with sleep. A "heavy ache" appeared in the limbs, culminating in a "spontaneous jerking" which was immediately preceded by a "sensation" spreading down the affected limb. The legs were principally affected, but the arms were also involved, though to a much less extent. "It seems to come on when I am relaxed, if I sit down in the evenings or in bed. When it starts I can't stop it except by getting up." The symptoms made their appearance between the third and sixth months of her pregnancies and endured in a greatly diminished form for varying periods after the confinements.

Pain Group

As the following cases illustrate, pain similar in character to that in the previous group can occur in the absence of myoclonus during waking hours. Myoclonus, however, is commonly present during sleep—a feature common to all the groups into which the disorder has been subdivided for the purpose of classification.

Case 9.—A man aged 54 first began to be troubled with recurring pain in his left leg shortly after partial gastrectomy for dyspepsia two years previously. "I can't sit still—no time before left leg starts aching—pain like toothache at its worst within half an hour. As soon as I lie down it starts. I walk round the bedroom night after night. Once I manage to get to sleep I am all right. My wife says that it is the left leg that keeps kicking out at night when I am asleep."

Case 10.—This patient, a man aged 58, had since his youth, and especially during the past 10 to 15 years, had "throbbing, heavy, burning pain in both legs from the knees down; terrific ache, immediately relieved by standing and walking; not too bad during the day because I am concentrating on the paper work." Crural pain was also present on awakening in the mornings. His daughter, a young medical practitioner, was also similarly afflicted. She said: "I am afraid to sit down in the evenings. Once I sit down I become aware of a burning pain in the legs. It used to be in my right leg only. I've got to get out of bed in the mornings to be relieved of the pain—I can't have breakfast in bed."

Case 11.—A woman aged 51 complained of pains in the legs—"no trouble during the day—I get them when sitting down in the evenings, but mostly in bed. It starts with a throb in the calves and gradually gets worse—becomes a gripping neuralgia pain. Suddenly goes to such a pitch I have to get out of bed, then it goes quite quickly. Sometimes I go to sleep and it wakes me up; at other times it starts directly I lie down." According to her husband her legs kick out in her sleep.

"Sleep-pain" Group

As already mentioned, the appearance of symptoms on relaxation is always delayed, the latency period varying from case to case. Evidently this latency period may be so long as not to give rise to any overt manifestations during waking hours. In these cases the pain is felt only immediately on waking in the mornings, or the pain may awaken the sufferer in the night. Weir Mitchell (1897) described

this variant, which he named "sleep-pain." "I find in my notebook some half-dozen cases of pain in the legs, never known during the day, and needing sleep as a conditioning factor. Whenever I have spoken of this disorder to the patient he is apt, if intelligent, to say: 'No; not pain; it is distress.' The cases are alike. A man is well in the day, walks, works, does as do others. Some time after he falls asleep he is awakened by aching in the legs, from the soles half-way to the knees. There is but one remedy —motion. He rises, walks for ten minutes, is eased, goes to sleep, and in an hour or two awakens to feel the distress and repeat the relieving exercise." Weir Mitchell then gives a well-documented case history.

Two of the cases described by Purdon Martin (1946) in his paper on "unexplained pains in the legs at night" can be clearly recognized as presenting typical features of "sleep-pain." Furthermore, it was noted in these cases that similar pains were apt to occur occasionally during the evenings under conditions of relaxation.

"Restless Legs" Group

In his excellent monographs on "restless legs," Ekbom (1945, 1950) states that the only clinical description of this condition he could trace in the past medical literature was one given by Theodor Wittmaack in 1861. Wittmaack evidently recognized the three essential elements of this syndrome: (1) A crural sensation defying description—"eine nicht näher zu beschreibende Empfiindung—ohne allen Schmerz—ohne Ziehen." (2) Restlessness of the limbs—"als wäre ein Geist der Unruhe in die Beine gefahren." (3) The occurrence at rest—"theils gegen Abend, besonders aber in Bett bis zum Einschlafen."

Minor forms of this disorder are undoubtedly common—Ekbom (1945) put it as high as 5% in a representative control group of the population—and rarely it can occasion a considerable amount of distress, when relief can only be obtained by getting up and walking up and down. The heredo-familial character, the exacerbating influence of pregnancy and anaemia, as also myoclonus in sleep—features which have already been mentioned as characteristic of the disorder as a whole—also apply to this group. Ekbom (1945) mentions the case of a soldier suffering from restless legs, "who sometimes kicked so violently during his sleep that his neighbours in the tent had to put up planks to protect themselves."

There is a unanimity among patients that some form of disagreeable sensation in the legs precedes the movements, that this sensation is unlike anything experienced in ordinary life, and that movement of the legs affords some relief. "It feels like internal itching," "it feels as though my legs were tied, so that I have to move them," testified some of Ekbom's (1945) patients; and these analogies help to convey something of the nature of this sensation. All agree that, while the desire to move the legs can be resisted for a while, a point is quickly reached when this becomes impossible.

The "restlessness" implied in the name is in the main of voluntary nature. Myoclonic jerking can, however, occur also during the waking state. Allison (1943), from personal experience, described the movements which occur in this syndrome—called by him "leg jitters"—as follows: "A combination of voluntary movement and involuntary jerks of the affected limbs. It has no relation to the sudden leg-jerk which sometimes occurs at the moment of going off to sleep." These references to myoclonus are of some importance, as they help to bridge the various subgroups.

"Dyslysis"

Underlying the graded series of cases presented here, there is clearly a neurological disorder showing several uniform features. That relaxation rather than immobility of the limbs is the provocative factor can be inferred from the fact that in most cases the symptoms may be absent or minimal while the sufferer is engaged in his business, even if the limbs remain immobile for a long time, as when the job is of a sedentary nature. Bearing in mind that the disorder is one attendant upon relaxation of the limbs, it may be justifiable, to avoid circumlocution, to speak of "dyslysimelia," making use of the classical Greek word "lysimelia" denoting a state of relaxation of limbs as in sleep or death. For reasons of brevity "dyslysis" may, however, be preferable.

Provocative and Aggravating Factors.—Excepting for pregnancy and anaemia, no obvious precipitating or aggravating factor could generally be discovered in the cases of dyslysis reviewed. In one case the onset of myeloid leukaemia was followed by a pronounced exacerbation. In a case of disseminated sclerosis of recent onset much distress was caused by dyslysis shortly afterwards.

Differential Diagnosis

Dyslysis can manifest itself during waking hours, during sleep, and during predormitium, which Weir Mitchell (1897) defined as follows: "As we are falling asleep the senses go off guard in an orderly and well-known succession—this interval I desire to label prae-dormitium." The symptoms of dyslysis commonly occur during waking hours, but may exceptionally occur only during sleep. However, in none of the cases reviewed here or quoted by others has there been an *exclusively* predormitial incidence. A great variety of sensory and motor disturbances are known to occur, often with regularity, during predormitium; but these phenomena, because of their exclusively predormitial incidence, should provisionally not be grouped with dyslysis. A further noteworthy nosographic point is the absence in dyslysis of tactile paraesthesiae such as pins-and-needles and numbness.

Acroparaesthesia.—The cardinal feature of this syndrome is the occurrence of paraesthesiae, with or without associated pain, in the upper limbs after the affected limbs have remained immobile for some time, either at rest or during activities in which there is little or no movement, as when writing, knitting, holding a newspaper or telephone receiver, etc. These symptoms as a rule are conspicuous at a time when objective sensory abnormalities are minimal or entirely absent. In early cases the immobility of the limbs has to be long-sustained so that the incidence is purely nocturnal, symptoms causing the patient to awake from sleep, or else the incidence is matutinal, symptoms becoming evident for a short time immediately on awakening in the mornings. Apart from the difference of the limbs principally involved —arms in acroparaesthesia and legs in dyslysis—there are also other diagnostic differences—for example, absence of tactile paraesthesiae in dyslysis, to be borne in mind.

Predormitial Myoclonus.—A sudden start of one or more limbs occurs not infrequently when falling off to sleep, and may arouse the sleeper. Weir Mitchell (1897) mentions the case of a woman whose sleep was rendered impossible by a series of such "explosions" each night. "Just as she begins to lose herself an arm, a leg, or the whole body suddenly moves with violence. As she awakens, hands and feet, or either alone, twitch for a few moments. Then she settles herself to sleep anew, only to repeat the same process." Because of the exclusively predormitial incidence these cases should be differentiated from dyslysis.

Nocturnal Burning Legs.—The descriptive name applied to this syndrome by Tinel (1937) was "causalgie nocturne spontanée de vieillards." It should be added that these distressing thermal paraesthesiae in the feet and legs eventually become continuous, disappearing only when walking. The thermal character and unremitting nature of the paraesthesiae during rest help to distinguish this condition from dyslysis.

Cases of dyslysis vary considerably in severity, but, clinically, two phases can be generally recognized: (1) latency phase, and (2) phase of overt clinical manifestations. During the latter phase there occurs rarely the phenomenon of sensory precipitation of myoclonus (Case 1).

Treatment

Most patients find that phenobarbitone appreciably relieves the symptoms of dyslysis. One patient who had been given phenobarbitone for some other condition reported that, while this treatment failed to effect the improvement expected, it considerably relieved her symptoms of dyslysis. Case 7 at first improved on phenobarbitone, but relapsed later. Iron therapy for the control of anaemia relieved dyslysis in a most dramatic fashion.

Conclusion

From the physiological point of view the disturbance of relaxation of limbs described in this paper is best regarded as "inhibition of inhibition." An analogy is provided by an experiment in which a recurrently elicited knee-jerk in a cat is first inhibited by ipsilateral sensory-nerve stimulation, and later this inhibition is "inhibited" by stimulation of the bulbar reticular formation (Bach, 1950).

The following points may perhaps indicate that dyslysis is a manifestation of a raised excitatory state referable to bulbar reticular activity: (*a*) exceptionally high voltage of motor unit potentials were observed during minimal effort contractions; (*b*) pronounced susceptibility of dyslysis to the influence of lowered oxygen tension; (*c*) the occasional sensory precipitation of myoclonus; (*d*) a partial improvement obtained in most cases with phenobarbitone.

Summary

A disorder characterized by disturbed relaxation of limbs at rest is described.

Cases are divided into the following groups, in accordance with the chief clinical features: myoclonus group, pain and myoclonus group, pain group, "sleep-pain" group, and "restless legs" group.

Legs are usually, but not always, the only limbs affected in this disorder, which often shows a heredofamilial incidence and tends to have a long, fluctuating course. Myoclonus during sleep is common.

Pregnancy and anaemia greatly aggravate this condition.

During the phase of overt manifestation of symptoms, sensory precipitation of myoclonus may occur.

Differential diagnosis and treatment are discussed.

"Dyslysis" is suggested as a name for this syndrome.

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"The speed with which people grow old depends as much on social factors as it does on purely physical processes. Ageing is quickened by such things as the loss of interests due to compulsory retirement or frailty; loss of relatives and friends due to the inevitable result of living longer; loss of financial security due to a decline in income or in the value of money; loss of emotional security due to changing environment; loss of status through ceasing to be primarily a contributor to society; and loneliness. Singly or collectively, these are responsible for much of the frustration, disappointment, anxiety, depression, and unusual behaviour amongst elderly citizens."—*Notes on Mental Frailty in the Elderly*, a booklet prepared by the National Old People's Welfare Council for the guidance of those concerned with the care of the elderly. The *Notes* (price 1s.) are obtainable from the National Council of Social Service, 26, Bedford Square, London, W.C.1.

STAPHYLOCOCCAL SPINAL MENINGITIS

BY

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During the years 1949–56, 115 cases of pyogenic meningitis were admitted to the isolation ward of the Cumberland Infirmary (Table I). Comparison of the

TABLE I.—*Pyogenic Meningitis*, 1949–56

Type of Infection	No. of Cases	No. of Deaths
Meningococcal	61	3
Influenzal	15	1
Pneumococcal	16	3
Pyogenic. No growth on culture	16	—
Staphylococcal	7	1
Total	115	8

figures in Table I with other published series showed an unusually high incidence of staphylococcal infection. These cases presented as meningitis without any obvious local sepsis, but, because of their probable relationship to staphylococcal epidural abscess, the term "staphylococcal spinal meningitis" is used to describe them.

Literature

The first proved case of staphylococcal meningitis was described by Galippe in 1889, following suppuration of the jaw. Anthony (1892) reported the first "cryptogenic staphylococcal meningitis" in a robust soldier aged 23. Neal (1924) and MacNeal *et al.* (1943) collected small series of cases, and Teng and Meleney (1950), in an exhaustive review of the literature, recorded 88 cases with recovery.

In approximately one-third of the published cases the source of infection has been described as "haematogenous" or unknown. The infecting organism, in all but a small minority, has been a coagulase-positive *Staphylococcus aureus*, but *Staph. albus, Staph. citreus*, and a mixture of organisms have been incriminated. The possibility of contamination of cerebrospinal fluid (C.S.F.) samples makes evaluation of all reported cases difficult, but the criterion adopted has been the presence of staphylococci in direct smears, and their growth on culture, in cases of pyogenic meningitis.

Prior to 1932 the only successes in treatment were reported from France, where it was recognized that many of the so-called primary infections were secondary to latent spinal infection. This type of case was called "la forme rachidienne primitive," and treated by laminectomy and drainage (Sicard and Paraf, 1925; Benoit, 1929; Chavany and George, 1929). Benoit (1929) recognized the danger that lumbar puncture may precipitate generalized meningitis and cautioned against unnecessary spinal taps.

Staphylococcal bacteriophage (Schless, 1932) was given intrathecally with some benefit, and sulphonamides alone (Tolan, 1943) assisted recovery in one case, but it was the introduction of penicillin by intrathecal and intramuscular injection, used in conjunction with sulphonamides, that first gave a prospect of cure in the majority of cases (Evans, 1944; McCune and Evans, 1944; Worth, 1945; Johnson and Walker, 1945). With the emergence of penicillin-resistant strains of organism, other antibiotics have been used with success. Intrathecal and intramuscular bacitracin (Teng and Meleney, 1950; Teng, 1950), chlortetracycline (Almklov and Hansen, 1949), and intrathecal and oral chloramphenicol (Anderson and Ellis, 1951) have all been proved of value in small numbers of cases.

Because of the high incidence of spinal block in cases of staphylococcal meningitis, streptokinase–streptodornase by

intrathecal injection has been advocated by Lièvre *et al.* (1952), but results in the treatment of tuberculous meningitis make it doubtful whether there is any place for the intrathecal use of this drug.

Present Series

The present series comprises seven patients (Table II), aged 18 months to 47 years, admitted to the isolation ward of a general hospital over the period 1949–56. The immediate past history was significant in four of them, but often leading questions were needed to obtain the information.

TABLE II.—*Age Incidence and Primary Site of Infection*

Case	Sex	Age	Possible Primary Site of Infection
1	F	11 years	Right hip bruised 14 days before admission
2	F	11 ,,	Not known
3	M	1½ ,,	Not known. L.P. by family doctor 8 days before admission
4	F	28 ,,	? Left perinephric cellulitis
5	M	47 ,,	Boil on neck 5 weeks before admission
6	F	3 ,,	Bruised left thigh 7 days before admission
7	F	29 ,,	Not known

In Case 3 the lumbar puncture by the family practitioner eight days before admission might at first sight be blamed as the cause of the infection, as he obtained a clear fluid with a normal cell count on that occasion but the child was already ill with a stiff neck and rigid back at that time. The same sequence was seen in Case 2: an 11-year-old girl was admitted with staphylococcal septicaemia, associated with severe neck and back stiffness. Initial lumbar puncture yielded clear C.S.F. with 1 cell per c.mm., yet five days later thick staphylococcal pus was aspirated from the same interspace. Both these cases confirm Benoit's (1929) warning that in the presence of staphylococcal septicaemia the stiff back and neck may be due to epidural rather than meningeal infection, and lumbar puncture may induce a generalized meningitis.

In Case 5 the boil on the neck five weeks previously was remembered only after cross-questioning. Both Case 1, with marked bruising of the right hip 14 days before admission, and Case 6, that of a little girl who fell off her tricycle seven days before admission and bruised her left thigh, seemed to suggest the possibility of local osteomyelitis, but no clinical or radiological confirmation of this was obtained. Case 4 was of interest. A 28-year-old woman presented with a history of left lumbar pain, vomiting, and pyrexia for five days. There was tenderness and guarding in the left renal area, but no neck stiffness. Microscopy of the urine showed no excess of pus cells, but the urine was coloured golden brown with urobilinogen. There was moderate anaemia (haemoglobin 10 g./100 ml.) and polymorphonuclear leucocytosis (80% of 22,000 white blood cells per c.mm.), and a presumptive diagnosis of perinephric cellulitis was made. Three days later there was a sudden onset of neck stiffness, and lumbar puncture revealed purulent staphylococcal meningitis, with a C.S.F. protein level of 2,600 mg./100 ml. The spontaneous rupture of an epidural abscess again seemed to be the likely explanation, but an initial perinephric cellulitis could not be excluded.

Clinical Picture

The overwhelming complaint in each case was of backache rather than headache, which was virtually absent in three cases. A striking feature was the absence of mental clouding, disorientation, and convulsions, and the picture was that of a predominantly spinal, rather than cerebral, irritation. Fever, generalized muscular pains, vomiting, and restlessness were commonly present, but the general condition was remarkably good for such an obviously severe infection. Rigors were not recorded by any case, even in the presence of a frank septicaemia.

Physical signs in the established case were those of meningitis with neck and back rigidity, and Kernig's sign was positive. Cases 1 and 6 had some limitation of hip movement and Case 4 left renal tenderness. In no case was there local vertebral tenderness or evidence of root irritation or cord compression. No obvious skin sepsis was present, and there was no evidence of cranial nerve involvement or papilloedema. The temperature on admission varied between 101 and 104° F. (38.3 and 40° C.), with an average of 102° F. (38.9° C.).

Blood examination showed a mild anaemia with an average haemoglobin level of 13.8 g./100 ml. in six cases, and a moderate haemolytic anaemia with haemoglobin level of 10 g./100 ml. in the seventh. There was a marked polymorphonuclear leucocytosis in each case, with white blood cell counts averaging 20,000 per c.mm., the highest being 33,700 per c.mm., but comparison with other forms of pyogenic meningitis showed that this had no real value in differential diagnosis. Blood culture was performed in five cases, and was positive for *Staph. pyogenes* in three.

In two cases normal C.S.F. was obtained on initial puncture, but in the established cases thick pus which had to be aspirated was found in four, and opalescent, xanthochromic fluid under reduced pressure in the remaining three cases (Table III). The sugar content of the C.S.F. was greatly reduced in every case, but insufficient fluid was obtained in the first sample to estimate it. The organism was a coagulase-positive *Staph. aureus* (*pyogenes*), and was seen in direct films and grew on culture in each case. In six cases it was fully sensitive to penicillin, the seventh being partially sensitive to penicillin and sensitive to chloramphenicol and the tetracyclines.

TABLE III.—*Initial C.S.F. Findings in Established Cases*

Case	Appearance and Polymorphs (per c.mm.)	Protein mg./100 ml.	*Staph. pyogenes*	Sensitivity
1	Thick pus. Xanthochromic	900	+	Penicillin
2	,, ,, Few drops	—	+	,,
3	,, ,, ,, ,,	—	+	,,
4	Clotted. Xanthochromic	2,600	+	Partial penicillin; chloramphenicol; tetracyclines
5	9,000	284	+	Penicillin
6	Thick pus. Few drops		+	,,
7	5,000. Xanthochromic	1,950	+	,,

X-ray films of the entire spine were negative in each case, the hip-joints were clear in Cases 1 and 6, and the intravenous pyelogram was normal in Case 4. Chest *x*-ray films were clear in four cases. Case 1 was initially clear, and later showed a small encysted empyema. Case 2 showed the classical appearance of staphylococcal pneumonia with a small spontaneous pneumothorax, and later "soap bubble" abscesses.

Treatment

The mainstay of treatment was the combination of intrathecal and intramuscular penicillin with oral or intramuscular sulphonamides. Intrathecal penicillin, in daily doses not exceeding 15,000 units, was given for an average of 10 days. A second course of intrathecal penicillin was given in the fourth week of illness in Case 3 following a full-scale relapse, and a modified course in Case 5 when the C.S.F. picture deteriorated.

In the earlier cases intramuscular penicillin was given in doses of 100,000 units three-hourly, and later in doses of up to 1 mega-unit four- to six-hourly for at least 21 days. The sulphonamides (sulphadiazine or sulphadimidine) were given orally unless there was severe vomiting, but the initial loading dose of 2 g. was given intramuscularly. Dosage varied with age between 4 and 6 g. daily for an average of 14 days. Crystalluria was not encountered.

In addition to this routine, streptomycin, 1 g. a day, was given in Case 3 for 13 days, chlortetracycline, 1 g. a day for 17 days, in Case 5, and chloramphenicol for short periods in Case 4, and for 20 days in Case 6.

Clinical Course

There was one death (Case 7). A 29-year-old woman was admitted with a five-day history of back pain associated with stiffness of the back muscles and fever. After three

days she developed frontal headache, and on the day of admission complained for the first time of a stiff neck. On examination she was toxic and ill, with a high fever (104° F. —40° C.) and rapid pulse (148 a minute). She showed gross back and neck stiffness, but no local bone tenderness or signs of cord compression. The C.S.F. was turbid and xanthochromic under markedly reduced pressure, and examination showed 5,000 polymorphs per c.mm., protein 1,950 mg./100 ml., and sugar 35 mg./100 ml. *Staph. pyogenes* was grown from both blood and C.S.F. culture. Treatment was started at once with 10,000 units of penicillin intrathecally, 1 million units intramuscularly, 2 g. of sulphadimidine and 1 g. of streptomycin intramuscularly. Despite this she died suddenly a few hours after admission. Necropsy (Dr. J. S. Faulds) showed multiple staphylococcal lung abscesses, a small splenic abscess, and severe toxic changes in liver and heart muscle. Detailed examination of the vertebrae failed to show any obvious osteomyelitis, and there was no epidural collection of pus. The meningeal changes were marked in the spinal canal, but much less obvious at the base of the brain, and virtually absent over the vertex.

This unexpected death was all the more tragic when it was found that the staphylococcus was fully sensitive to penicillin.

In the other cases the temperature settled in 10–16 days, and the C.S.F. became sterile in three to nine days. In Case 3 relapse occurred at one month, after the temperature had been normal for a fortnight and treatment discontinued for a week. This patient responded well to a second full course of treatment. In Case 1 a small sterile empyema required aspiration, and in Case 3 staphylococcal pneumonia developed with a small left-sided spontaneous pneumothorax. Both these cleared well without residual signs. In Case 5, after one month, the patient still had a polymorphonuclear pleocytosis in the C.S.F. and continued headache, but made slow progress and recovered completely in six weeks. In Case 6 measles developed on the ninth day in hospital, but the patient suffered no more than a temporary setback.

The time in hospital varied from 23 to 60 days, with an average of 40 days. The condition on discharge was excellent and was maintained on routine follow-up.

Discussion

The predominantly spinal localization of the meningitis in this series makes the theory that this form of meningitis is secondary to epidural suppuration attractive. However, Hulme and Dott (1954) state that epidural spinal abscess follows a fairly constant pattern: (1) constant spinal ache; (2) root pain of the affected trunk; (3) impairment of cord function leading to sphincter disturbances and early motor and sensory loss; and (4) complete paralysis.

As no case in this series showed any sign of root irritation, and the one case coming to necropsy, although presenting with obvious C.S.F. loculation, had no evidence of any sizable abscess, there is no clear confirmation of this theory. Four cases did, however, develop sudden neck stiffness after a variable period of severe back pain, and in two of these the initial C.S.F. had been clear. In the absence of any obvious vertebral osteomyelitis, it seems reasonable to postulate spread from the epidural space, perhaps accelerated by lumbar puncture in two cases, as the probable explanation. Therefore it is felt that these cases should be watched closely for the earliest sign of root pain, cord compression, or localized spinal tenderness, when they should be referred to a neurosurgical clinic without delay.

The finding of so many strains of staphylococcus fully sensitive to pencillin may not be usual, and in future wide-spectrum antibiotics may cut out the need for intrathecal injections of penicillin, but the routine followed was so successful that it seems justifiable to treat penicillin-sensitive organisms along these lines in future.

Summary

Seven cases of staphylococcal spinal meningitis are described. One patient died within a few hours of admission; the remaining six made a full recovery.

The predominantly spinal localization of the meningitis is stressed and its relationship to epidural abscess discussed.

My thanks are due to Dr. J. S. Faulds, who carried out the necropsy in Case 7.

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TABLE FOR ASCERTAINING WHETHER DIFFERENCES BETWEEN PERCENTAGES ARE STATISTICALLY SIGNIFICANT

BY

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Smyth and Bainbridge (1957) suggest a scheme of tabulating data and thereby ascertaining whether any two factors concerning a group of patients are related. This they do by calculating the statistical significance of the difference between the percentage incidence (Pa) of one of the factors (a) and of the percentage incidence of both factors combined (Pab/b). The latter percentage is calculated by dividing the actual incidence of the combination of both factors (Nab) by the actual incidence of factor b—that is, Nb.

If the difference between Pa and Pab/b exceeds 1.96 times its standard error, then the difference is significant at the 5% level, and thus there are 19 chances out of 20 that the two factors are related. The standard error (S.E.) of the difference is given by:

$$S.E. = \sqrt{Pa(100-Pa)\ (1/Nb-1/N)}$$

where N=total number of patients (Yule and Kendall, 1950). It is therefore possible to tabulate values of 1.96 times the S.E. for various values of Pa and of (1/Nb−1/N). This has been done in the accompanying table. By using this table it is possible to find whether the difference between Pa and Pab/b is significant without having to work out the S.E. When there are many such differences the table should save a considerable amount of time.

Method of Use

To use the table, the percentage incidence of each factor (Pa, etc.) should first be calculated. These are the diagonal percentages in Smyth and Bainbridge's diagram. Then (1/Nb−1/N)=n should be calculated for each factor. This

Table of D Significant at 5% Level-Percentages

Pa = or	0·5 99·5	1·0 99·0	1·5 98·5	2·0 98·0	3 97	4 96	5 95	6 94	7 93	8 92	9 91	10 90	12 88	14 86	16 84	18 82	20 80	25 75	30 70	35 65	40 60	45 55	50% 50%
n = 0·100	4·38	6·17	7·54	8·68	10·6	12·2	13·6	14·8	15·9	16·9	17·8	18·6	20·2	21·6	22·8	23·9	24·8	26·9	28·5	29·6	30·4	30·9	31·0
0·095	4·27	6·02	7·35	8·46	10·4	11·9	13·2	14·4	15·5	16·4	17·3	18·2	19·7	21·0	22·2	23·3	24·2	26·2	27·7	28·9	29·6	30·1	30·3
0·090	4·15	5·86	7·15	8·24	10·1	11·6	12·9	14·0	15·1	16·0	16·9	17·7	19·2	20·5	21·6	22·6	23·6	25·5	27·0	28·1	28·9	29·3	29·5
0·085	4·04	5·69	6·95	8·01	9·75	11·2	12·5	13·6	14·6	15·6	16·4	17·2	18·6	19·9	21·0	22·0	22·9	24·8	26·2	27·3	28·0	28·5	28·6
0·080	3·91	5·52	6·74	7·77	9·46	10·9	12·1	13·2	14·2	15·1	15·9	16·7	18·1	19·3	20·4	21·3	22·2	24·1	25·5	26·5	27·2	27·6	27·8
0·075	3·79	5·35	6·53	7·52	9·16	10·6	11·7	12·8	13·7	14·6	15·4	16·2	17·5	18·7	19·7	20·7	21·5	23·3	24·6	25·7	26·3	26·7	26·9
0·070	3·67	5·16	6·31	7·27	8·85	10·2	11·4	12·4	13·3	14·1	14·9	15·6	16·9	18·0	19·1	20·0	20·8	22·5	23·8	24·8	25·5	25·8	26·0
0·065	3·53	4·98	6·08	7·00	8·53	9·80	10·9	11·9	12·8	13·6	14·4	15·0	16·3	17·4	18·4	19·2	20·0	21·7	22·9	23·9	24·5	24·9	25·0
0·060	3·39	4·78	5·84	6·73	8·20	9·41	10·5	11·5	12·3	13·1	13·8	14·5	15·7	16·7	17·7	18·5	19·3	20·8	22·1	22·9	23·6	23·9	24·1
0·055	3·25	4·58	5·59	6·44	7·85	9·01	10·1	11·0	11·8	12·5	13·2	13·8	15·0	16·0	16·9	17·7	18·4	20·0	21·1	22·0	22·6	22·9	23·0
0·050	3·10	4·37	5·33	6·14	7·48	8·59	9·56	10·5	11·2	11·9	12·6	13·2	14·3	15·3	16·1	16·9	17·6	19·0	20·1	21·0	21·5	21·9	22·0
0·045	2·94	4·14	5·06	5·83	7·10	8·15	9·07	9·88	10·7	11·3	11·9	12·5	13·6	14·5	15·3	16·0	16·7	18·1	19·1	19·9	20·4	20·7	20·8
0·040	2·77	3·91	4·77	5·49	6·69	7·69	8·55	9·31	10·1	10·7	11·3	11·8	12·8	13·7	14·4	15·1	15·7	17·0	18·0	18·7	19·3	19·6	19·7
0·035	2·59	3·65	4·46	5·14	6·26	7·19	8·00	8·71	9·36	9·95	10·5	11·1	12·0	12·8	13·5	14·1	14·7	15·9	16·9	17·5	18·0	18·3	18·4
0·030	2·40	3·38	4·13	4·76	5·80	6·66	7·40	8·07	8·67	9·22	9·72	10·2	11·1	11·8	12·5	13·1	13·6	14·8	15·6	16·2	16·7	16·9	17·0
0·025	2·19	3·09	3·77	4·34	5·29	6·08	6·76	7·36	7·91	8·41	8·87	9·30	10·1	10·8	11·4	12·0	12·4	13·5	14·3	14·8	15·2	15·5	15·5
0·020	1·96	2·76	3·37	3·89	4·73	5·44	6·05	6·59	7·08	7·52	7·94	8·32	9·01	9·62	10·2	10·7	11·1	12·1	12·8	13·3	13·6	13·8	13·9
0·015	1·70	2·39	2·92	3·37	4·10	4·71	5·24	5·71	6·13	6·52	6·87	7·21	7·81	8·33	8·81	9·23	9·61	10·4	11·1	11·5	11·8	12·0	12·1
0·010	1·39	1·96	2·39	2·75	3·35	3·85	4·28	4·66	5·01	5·32	5·61	5·89	6·37	6·81	7·19	7·54	7·85	8·49	8·99	9·35	9·61	9·76	9·81
0·008	1·24	1·75	2·14	2·46	3·00	3·44	3·83	4·17	4·48	4·76	5·02	5·26	5·70	6·09	6·43	6·74	7·02	7·60	8·04	8·37	8·59	8·73	8·77
0·006	1·08	1·52	1·85	2·13	2·59	2·98	3·31	3·61	3·88	4·12	4·35	4·56	4·94	5·27	5·57	5·84	6·08	6·58	6·96	7·25	7·44	7·56	7·60
0·004	0·875	1·24	1·51	1·74	2·12	2·43	2·71	2·95	3·17	3·37	3·55	3·72	4·03	4·31	4·55	4·77	4·96	5·37	5·69	5·92	6·08	6·17	6·20
0·002	0·619	0·873	1·07	1·23	1·50	1·72	1·92	2·09	2·24	2·38	2·51	2·63	2·85	3·05	3·22	3·37	3·51	3·80	4·02	4·19	4·30	4·37	4·39
0·001	0·438	0·617	0·754	0·868	1·06	1·22	1·36	1·48	1·59	1·69	1·78	1·86	2·02	2·16	2·28	2·39	2·48	2·69	2·85	2·96	3·04	3·09	3·10
0·0005	0·310	0·437	0·533	0·614	0·748	0·859	0·956	1·05	1·12	1·19	1·26	1·32	1·43	1·53	1·61	1·69	1·76	1·90	2·01	2·10	2·15	2·19	2·20
0·0001	0·139	0·196	0·239	0·275	0·335	0·385	0·428	0·466	0·501	0·532	0·561	0·589	0·637	0·681	0·719	0·754	0·785	0·849	0·899	0·935	0·961	0·976	0·981
0·00001	0·044	0·062	0·076	0·087	0·106	0·122	0·136	0·148	0·159	0·169	0·178	0·186	0·202	0·216	0·228	0·239	0·248	0·269	0·285	0·296	0·304	0·309	0·310
0·000001	0·014	0·020	0·024	0·028	0·034	0·039	0·043	0·047	0·051	0·054	0·057	0·059	0·064	0·069	0·072	0·076	0·079	0·085	0·090	0·094	0·097	0·098	0·099

may easily be done by using a slide rule or a table of reciprocals. Then any calculated difference—for example, $|Pa-Pab/b|$—may be immediately compared with the appropriate value in the table. If the calculated difference (D) is equal to or exceeds the appropriate tabulated D, then the calculated D is significant.

The actual values of Pa and of n will not usually coincide with the tabulated values of Pa and n respectively, but the actual values will each lie between two adjacent tabulated values. When this is the case, four values of D will be obtained from the table, corresponding to the two adjacent tabulated values of both Pa and n. If the calculated D is greater than or equal to the largest of these four tabulated Ds, then the difference is significant. If the calculated D is less than the smallest of the four tabulated Ds, then the difference is not significant. In practice the calculated D will seldom fall within the range of the four tabulated Ds. But when this does occur it will be necessary to interpolate. An example will make the appropriate procedure clear.

Let $Pa=33.1\%$, $Nb=21$, and $N=504$. Thus $1/Nb-1/N=n=0.0476-0.0020=0.0456$. Now Pa lies between 30 and 35 and n lies between 0.045 and 0.050. The four values of D corresponding to these values of Pa and n are as follows: 19.1, 19.9, 20.1, and 21.0. Thus if the calculated D is equal to or greater than 21.0, then it is significant, but if D is less than 19.1, then it is not significant. But if the calculated D is 19.3, for example, then we must interpolate. To do this, take $n=0.045$ and note that for $Pa=30\%$, D is 19.1, and for $Pa=35\%$, D is 19.9. Thus for $n=0.045$ and $Pa=33.1\%$, $D=19.1+\frac{33.1-30.0}{35.0-30.0}(19.9-19.1)=19.1+\frac{3.1\times0.8}{5}=19.1+0.5=19.6$.

Now take $n=0.050$. For $Pa=30\%$, D is now 20.1 and for $Pa=35\%$, D is 21.0. For $n=0.050$ and $Pa=33.1\%$, D therefore $=20.1+\frac{33.1-30.0}{35.0-30.0}(21.0-20.1)=20.1+\frac{3.1\times0.9}{5}=20.1+0.6=20.7$. Thus for $n=0.0456$ and $Pa=33.1\%$, $D=19.6+\frac{0.0456-0.0450}{0.0500-0.0450}(20.7-19.6)=19.6+\frac{0.0006\times1.1}{0.0050}=19.6+\frac{0.66}{5}=19.6+0.1=19.7$. Thus if the calculated D is equal to or greater than 19.7 it is significant at the 5% level. The figure 19.7 is the same as is obtained if the S.E. is worked out in the usual way and multiplied by 1.96.

The table should not be used if Pa or $(100-Pa)$, whichever is smaller, multiplied by Nb or $(N-Nb)$, whichever is smaller, is less than 500. This figure seems large, but it is really a percentage. It corresponds to an actual number of only 5. If the smallest product is less than 500, then a more accurate method of testing significance should be used (see Fisher and Yates, 1948).

I should like to thank Professor Martin Roth, professor of psychological medicine, University of Durham, for bringing this matter to my attention.

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A new feature of the Royal Society of Health's annual congress is to be a section devoted to Radiation. This will be introduced at Harrogate next April. The existing Tropical Hygiene Section will be amalgamated with the World Health Section under the new title "World Health including Tropical Hygiene." Provision has also been made for a Conference of Health Visitors in addition to a separate Conference of Domiciliary Nurses and Midwives.

HAEMOGLOBIN O (BUGINESE X) IN SULAWESI

BY

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In 1956 the finding of what might be a new haemoglobin in the Buginese in Sulawesi (formerly Celebes) was reported (Lie-Injo, 1956). This report, however, did not attract any attention as it was written in the Indonesian language. In the meantime the haemoglobin has been studied more extensively by laboratories in other parts of the world, and we all agree that it is not identical with any other known haemoglobin. In this paper we record the results of further study.

Physico-chemical Properties

In 1956 the electrophoretic mobility of this haemoglobin at *p*H 8.6 was described as being between that of Hb S and Hb E (see Fig.). In phosphate buffer *p*H 6.5 it was slightly slower than Hb S and Hb C. It was not alkali-resistant, and the erythrocytes containing it gave negative sickling tests on repeated examinations. It occurred in addition to normal haemoglobin in the blood and was always present in a low concentration.

Paper electrophoresis showing Hb O compared with Hb A, E, and S at *p*H 8.6.

After repeated examinations it was not so easy to establish the exact electrophoretic mobility of the abnormal component. It was thought to be partly due to the low concentration (Lie-Injo, 1957). Study of this haemoglobin, which had provisionally been called Hb Buginese X, by three different well-known experts in three different countries did not make the problem easier, as all three had a different opinion regarding its electrophoretic mobility.

Recently a large amount of blood containing Hb Buginese X was obtained from the blood bank in Djakarta (Java), and large samples were again sent to different laboratories. Dr. H. Lehmann, of London, found that Hb Buginese X at *p*H 8.6 had a mobility between that of the Hb S and Hb E just as originally published by one of us in 1956 (Lie-Injo, 1956). He is of the opinion that our haemoglobin is indeed a new haemoglobin.

Dr. T. H. J. Huisman, of Holland, examined our haemoglobin by different methods and came to the conclusion that it was not identical with any other known haemoglobin. On examining Buginese X chromatographically with "amberlite IRC-50" he found that it moved faster than Hb L but was slightly slower than Hb S. Also, with his newly developed chromatographic method using carboxymethyl cellulose, he again found that our haemoglobin differed from other known haemoglobins. Dr. H. A. Itano, of Bethesda, Maryland, examined it in the Tiselius apparatus

in cacodylate buffer *p*H 6.5, and stated that it was not identical with Hb C, Hb S, Hb D, or Hb G. However, to our surprise, he said that Buginese X in this buffer moved more rapidly than Hb S and Hb D. We have found, on repeated examinations by paper electrophoresis, that Buginese X in phosphate buffer *p*H 6.5 was slower than Hb C, Hb S, and Hb D. One wonders whether the difference in findings at *p*H 6.5 was due to the different buffers or the different supporting media used.

Dr. Itano also examined our haemoglobin in the Tiselius apparatus in barbitone buffer of *p*H 8.6, ionic strength 0.1 and found that it migrated more rapidly than Hb E and C and more slowly than Hb S, in both the ascending and the descending limbs. This finding is in agreement with ours on paper electrophoresis with the same buffer of the same *p*H.

As it has been confirmed by different laboratories that Buginese X differs from all other known haemoglobins, it should be allotted a letter. N was the letter most recently used to designate haemoglobin Liberian I (personal communication by Dr. James V. Neel). So far as we know, the letter O has not yet been used, and therefore Buginese X should be called Hb O. Dr. James V. Neel agreed with this choice.

Distribution and Incidence of Hb O

Haemoglobin O has so far been found only in persons who originate from the Indonesian island of Sulawesi. The only blood specimen containing Hb O obtained in Djakarta was from a pure Buginese from Sulawesi. We have found Hb O in the following ethnic groups:

6	Hb O carriers	among	455	Buginese in South Sulawesi
3	"	"	136	Makassars in South Sulawesi
1	"	"	107	Gorontalo in North Sulawesi
1	"	"	77	Toradjas who originate from Central Sulawesi but who were living in Makassar.

Thus Hb O is not very rare on this island. In the south the incidence is more than 1% in the Buginese. However, we did not find it among 233 Minahassers in North Sulawesi. In the Buginese and Makassars Hb E was also found in a low incidence.

Heredity.—We have not been able to conduct family studies in our Hb O carriers. However, after close inquiry it was found that the three Makassars who were Hb O carriers were related.

Haematological Study

A haematological study was difficult to carry out because of lack of adequate laboratory facilities in Sulawesi. The blood was to be flown to Djakarta directly after it had been drawn, but the persons who were to do this always failed to arrive at the time scheduled by us. We were therefore able to examine only two of the carriers. In Mrs. Sal the data obtained (see Table) were within normal limits: only the resistance of the erythrocytes to hypotonic saline solutions was increased. In Mrs. Muna there was a slight anaemia. However, her blood contained malaria parasites. In Mrs. Muna also the resistance of the erythrocytes was increased. The peripheral blood of both women did not show obvious changes, and did not resemble the picture we usually see in thalassaemia-trait carriers. Anisocytosis and poikilocytosis, when present, were very slight indeed. Target cells were very rare and no stippled cells were seen.

Details of Two Carriers

	Mrs. Sal	Mrs. Muna
Age in years when examined	35	30
Hb (g./100 ml.)	13·2	11·0
R.B.C. per c.mm.	5,230,000	4,300,000
Packed cell volume (%)	42·0	—
M.C.V. (cubic microns)	80·3	—
M.C.H. ($\mu\mu$g.)	24·9	—
M.C.H.C. (%)	31·4	—
Leucocytes per c.mm.	6,100	—
Differential count of W.B.C.	Normal	Normal
Poikilocytosis and anisocytosis	±	±
Target cells	Very rare	Very rare
Saline fragility: Initial at	0·44	0·44
Saline fragility: Complete at	0·20	0·20
Serum bilirubin	Not increased	Not increased
Alkali-resistant haemoglobin % of total (Singer's technique)	0·6	0·8
Hb analysis	A+O	A+O
Malaria	Negative	Positive

We are trying to get hold of the other Hb O carriers, and we hope to be able to give more details regarding them and their families in the near future.

Summary

The physico-chemical properties of Hb O (Buginese X) are described. The distribution and incidence of this haemoglobin are reported and the haematological findings in two Hb O carriers are presented.

We thank Dr. T. H. J. Huisman and Professor J. H. P. Jonxis, of Holland, Dr. H. Lehmann and Dr. J. A. M. Ager, of London, and Dr. H. A. Itano, of the U.S.A., for studying this haemoglobin and for their kind co-operation which made this publication possible. Thanks are also due to all colleagues and personnel who have helped to collect the blood specimens in Sulawesi. We are grateful to the Red Cross Blood Transfusion Service, Djakarta, especially to Miss Emmy Zachari, who sent us a large amount of blood containing haemoglobin O.

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Medical Memoranda

Unusual Reaction to Chlorpromazine

As chlorpromazine is being increasingly prescribed both in hospitals and by general practitioners, the rare toxic reaction described below seems worth reporting.

CASE REPORT

A youth of 20 attended the psychiatric clinic with the complaint that for a month he had been feeling "muddled up in his mind." As there was a strong family history of schizophrenia it was thought that he might be developing this disease. Chlorpromazine, 100 mg. thrice daily, was prescribed and he was asked to return in a fortnight. However, he was brought back to the clinic in a week by his father with the story that for the past two days he had had attacks in which—to quote the father—"he had horrible poses of his head and neck." Two attacks occurred in the clinic, each seeming to be precipitated by the stress of questioning. In the attack his head was drawn slowly backwards and to the right, and his shoulders became hunched up; the facial muscles, and to a less extent those to the neck and shoulder, underwent slow writhing movements; he was unable to speak but appeared fully conscious and was able to indicate that he understood what was said to him. The first attack lasted about 10 minutes, the second about 20 minutes. The postures were not identical in the two attacks. There was no tremor or clonic movement, nor was there difficulty in walking. In the intervals between the attacks the patient seemed quite unconcerned about them and said they caused him no anxiety or pain.

The father volunteered the information (which the patient confirmed) that two days previously the patient had taken six of his tablets at the same time—that is, 600 mg. of chlorpromazine—"in order to get some sleep." The attacks began about 12 hours after this.

The patient was admitted to hospital. He had several further attacks during the evening but then no more. Examination of his nervous system next day, and of his cerebrospinal fluid and skull x-ray film, revealed no

abnormality. He was discharged home after three days, and when seen at the clinic a fortnight later said he felt much better mentally. He was advised to resume chlorpromazine but would not do so.

COMMENT

There appear to have been only two reports of similar reactions after chlorpromazine. Labhardt (1954) mentions two patients, one a neurotic and one a psychopath, who showed "hysteriform" symptoms resembling *arc en cercle* and spasmodic torticollis, but gives no further information. Ayd (1956) describes the case a 16-year-old girl receiving 300 mg. of chlorpromazine daily who on the twelfth day suddenly developed dysarthria, facial grimacing, and involuntary muscle movements. She began taking chlorpromazine again three days later and had no recurrence of dystonia.

This type of reaction, very rare with chlorpromazine, appears to be less rare with the related drug prochlorperazine ("stemetil"). As one of the recognized toxic effects of both chlorpromazine and prochlorperazine is a parkinson-like syndrome, it is perhaps not altogether fanciful to picture the dystonic syndrome described here as in some ways analogous to the oculogyric crises of post-encephalitic parkinsonism.

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A Guided and Guarded Trephine for Bone-marrow Biopsy

There are many conditions in which histological examination of bone marrow may give information not obtainable by the examination of films made from material aspirated from the bone-marrow cavity.

Sometimes very small masses of marrow are withdrawn by needle puncture, and these may be picked out from the material aspirated and sections made from them. A small trephine, 5 mm. in diameter, may be driven into the sternum after an incision to obtain small portions of bone marrow (Dameshek, 1935). The specimens obtained, however, may be much too small for adequate histological study.

A larger trephine may be used at open operation on the sternum (Custer, 1949), a portion of rib may be excised (Hutt, Smith, Clark, and Pinniger, 1952), or a wedge of the crest of the ilium may be removed (Leonard, Israëls, and Wilkinson, 1957).

There is need for an instrument which will always produce an adequate amount of bone marrow for histological study from a part of the skeleton where red bone marrow is always present, without crushing of the specimen, without danger of damage to important structures, with the scar in an inconspicuous position, and by a method which is acceptable to the patient as a relatively minor diagnostic procedure that may be repeated at intervals, if desirable, to observe changes in the bone marrow with time or treatment. The instrument here described was designed in an attempt to fulfil these requirements.

It is unlikely that any method will be devised for obtaining an adequate amount of bone marrow without open operation.

The instrument consists of a combined guide and guard, and a trephine with a hole up the handle into which the guide fits (Fig. 1). Two trephines are available, 15 mm. and 11 mm. in diameter, the smaller one being more suitable for the narrower ribs of female patients.

A portion of rib is exposed posteriorly, and the periostium is reflected from the outer surface and also from the inner surface to about half-way down the width of the rib. The tongue of the guard is inserted in a vertical direction behind the rib, with the guide firmly pressed against the upper border of the rib. The trephine is then placed over the guide and, by pressure and rotation, is driven home against the guard. Care must be taken to saw through the bone, and not to use too much pressure, or the bone marrow may be crushed, rendering it useless for histological study. An

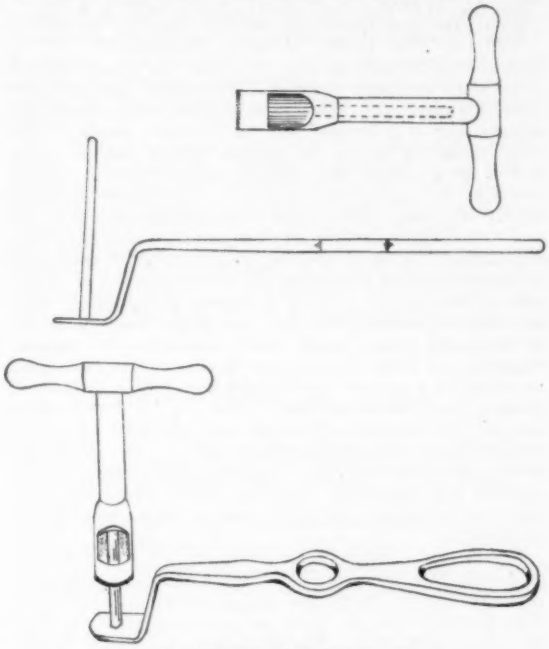

FIG. 1.—Diagram of the instrument.

instrument which is designed to bite out portions of bone is unsuitable because of the crushing of the marrow which occurs. The guard and trephine are then removed together. A portion of the upper margin of the rib, of the whole thickness of the rib, and nearly semicircular in shape, is thus obtained (Fig. 2). Contact smears or films can be made from the cut surface of the bone marrow and the semicircular disk of rib then placed in fixative and processed in the usual way.

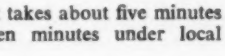

FIG. 2.—Actual size of sections obtained with the two trephines.

If the patient's condition warrants it, the operation is best done under general anaesthesia as advised by Hutt *et al.* (1952). It takes about five minutes under general anaesthesia and ten minutes under local analgesia.

Not once, either in the post-mortem room or in the operating theatre, has a rib been broken or the pleura damaged.

I am grateful to Professor W. St. C. Symmers and his staff of the Department of Morbid Anatomy, Charing Cross Hospital Medical School, for facilities, and particularly to Dr. Rosalinde Hurley for obtaining many of the post-mortem specimens. I am grateful to Mr. A. R. Makey for carrying out the biopsies.

The prototype of the instrument was made in soft metal by Alan Hickling, mechanical sciences undergraduate, Cambridge University, from which the instrument was made in stainless steel by the London Splint Company Limited, 67–69, Weymouth Street, London, W.1.

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Reviews

PRINCIPLES OF EPIDEMIOLOGY

Principles of Epidemiology. By Ian Taylor, M.D., M.R.C.P., D.P.H., and John Knowelden, M.D., D.P.H. (Pp. 300+vii; illustrated. 30s.) London: J. and A. Churchill, Ltd. 1957.

Epidemiological methods have in recent years been applied to the study of a wide range of diseases other than the communicable infections. This wider interpretation and use of epidemiology is in keeping with its definition, which is "the study of disease among the people," and it may be noted that in the middle of last century, when infections were so prevalent and deadly, the founders of the Epidemiological Society of London realized the value of epidemiology in the study of diseases like the dancing mania, apoplexy, goitre, and beriberi. With the growing awareness of the usefulness of epidemiological techniques for the elucidation of causes and the consequent control of disease the available tools have been sharpened and new ones introduced. Statistical methods are being taught more commonly to medical students, and many investigators in clinical and laboratory medicine are now making intelligent use of these methods in planning and evaluating their studies. A handbook which can be read and understood by such amateurs was sorely needed, and in *Principles of Epidemiology* Drs. Taylor and Knowelden have given us a primer which can be easily digested and assimilated. It is the aperitif which many will enjoy before tackling the more solid textbooks on statistical methods.

In the early chapters the methods for recording and analysing data are described, and particular emphasis is given to the collection and evaluation of morbidity data with the attendant limitations as well as advantages. Incidentally it seems a pity that the authors have not used morbidity rather than mortality data in illustrating the value of mass immunization against diphtheria, since mortality rates in many infectious diseases besides diphtheria show precipitous falls, although morbidity (unlike that in diphtheria) has changed very little.

The greater part of the book deals with the epidemiology of infectious diseases, which are used as models because they have been studied much more intensely than non-infectious diseases. Current beliefs about sources and modes of infection, host reactions and artificial immunization, the effects of environment and climate and of crowding and dispersal in the family or other community at risk are lucidly described with apt examples and simple charts or line drawings. This is no scissors-and-paste compilation; it is a well-illustrated story by two experienced "shoe-leather" epidemiologists, and it should, and I hope will, be widely read by many doctors in many lands.

ROBERT CRUICKSHANK.

PARTHENOGENESIS AND POLYPLOIDY

Parthenogenesis and Polyploidy in Mammalian Development. By R. A. Beatty. (Pp. 131+xi; illustrated. 15s.) London: Cambridge University Press. 1957.

The discovery of the chromosome mechanisms normally involved in the maturation of the gametes, in fertilization, sex determination, and the first cleavage division led to somewhat rigid ideas as to the regularity of the processes concerned. These ideas have received various shocks in the last decade, and Dr. Beatty's book on parthenogenesis and polyploidy indicates the ways in which the origin of a new individual may be atypical. Four categories of abnormality are listed: polar body formation may fail at either the first or second meiosis of the egg, the egg may be activated without fertilization, and the first mitotic division may not be completed by cytoplasmic cleavage. In all, 16 possible routes of development exist, distinguished by the number and origin of the chromosomes. Only one of these routes is strictly normal; eight of them relate to failure of fertilization. Even this catalogue does not exhaust the full possibilities of abnormality; for instance, androgenesis, development of a new individual from the egg cytoplasm and the spermatozoon nucleus only, is theoretically possible and occurs in some lower forms of life. These possibilities are now fully recognized, but are usually regarded as fantastically improbable in mammals. For the most part, however, methods for detecting their occurrence have been lacking, and the revelations which have followed Murray Barr's discovery of sex chromatin provide a good example of the queer things that appear when a new diagnostic tool becomes available. Perhaps the most interesting part of Dr. Beatty's book concerns recently developed methods of detecting anomalies of fertlization and early development, and the many reports relating to mammals are scrutinized in the light of modern information and against the background of events in lower organisms.

It seems that there is as yet no conclusive evidence that spontaneous development along any other route than the typical one has led to the birth of a normal living mammal. But, to the casual observer, what would the evidence be? To take extreme examples, if parthenogenesis occurred in a married woman it would never be suspected; in an unmarried woman it would never be believed. If a man produces a dozen daughters in a row he is regarded as chronically unlucky rather than chromosomally abnormal. The application of new knowledge and new methods to large samples of human material may yield results of great interest to the biologist, though perhaps perplexing to the individuals in question. Moreover, the increasing level of the assorted radiations and the increasing potency of the drugs to which the human race is now subjected are not likely to decrease the incidence of genetic whimsies. Who knows how many human parthenogens and polyploids are alive to-day, or how their numbers will increase in the atomic and pharmaceutical age now developing?

A. S. PARKES.

CHLORAMPHENICOL AND THE TETRACYCLINES

The Clinical Application of Antibiotics. By M. E. Florey, M.D. Volume III: *Chloramphenicol and the Tetracyclines*. (Pp. 393+ix. 84s.) London, New York, Toronto: Oxford University Press. 1957.

This volume is a continuation of the author's previous work *The Clinical Application of Antibiotics—Penicillin*, and like the earlier volume is a comprehensive and well-documented examination of the subject. The vast literature has not daunted the author, and although in the preface she regrets that the survey has not been so thorough as was the case with penicillin, because of "the phenomenal growth of written articles during the last few years," nevertheless the bibliography cited takes just over 40 pages and includes references up to June, 1956.

Separate sections are devoted to each of the four antibiotics—chloramphenicol and the three tetracycline compounds. In each section there is a chapter on general considerations, such as antibacterial action, complications of therapy, and methods of administration, followed by two chapters dealing respectively with "The Treatment of Diseases due to Specific Organisms" and "The Treatment of Diseases considered by Systems, Age, and Sex." Almost every condition for which these antibiotics have been used is mentioned, including diseases of doubtful aetiology, such as glandular fever, lupus erythematosus, and Hodgkin's disease. This wealth of material makes it a little difficult in places to see the wood for the trees, and the inexperienced clinician may find it difficult to discover appropriate treatment for a given infection owing to the fact that each antibiotic is dealt with in more or less watertight sections. The treatment of diseases for which the antibiotic under discussion is of particular value is, however, given in some detail. In any case the book is a mine of information and will be invaluable to all serious students of the subject.

MARY BARBER.

WAR MEDICAL HISTORY

Medical History of the Second World War. The Army Medical Services. By F. A. E. Crew, F.R.S. *Campaigns*—Volume II. (Pp. 537+xxxvii; illustrated. 84s.) London: H.M. Stationery Office. 1957.

This second volume follows the general pattern of Volume I reviewed in the *Journal* of June 15, 1957. One can only presume that strict adherence to medical ethics necessitates the complete anonymity of the principal characters, the theme "No names no pack drill" being rigidly followed throughout. The opening chapters of the war with Japan in Hong Kong and Malaya bring home to those fortunate enough not to have been involved in those terrible disasters the realization that the label "Prisoner of war in Japanese hands" meant more than a hell on earth. The main story of "The Bridge over the River Kwai" was only founded on fact; in these descriptions we have the facts—stark, staring facts—most moderately put with a restraint typical of the British habit of understatement. It is surprising not that there were so many deaths (murders) to be laid at the door of the Imperial Japanese Army, to its lasting disgrace, but rather that so many prisoners survived their tragic ordeal. A fine picture is painted of the endurance, resource, and resiliency of combatant and non-combatant alike. Many a "silk purse" was made out of material even less useful than a sow's ear. Professor Crew is to be congratulated on welding into a factual story the very scanty yet eyewitness accounts available to him.

The final saga of the war in Libya and North-West Africa is well told. The critical balance between victory and defeat at Alamein, the intransigent attitude of the responsible authorities in failing to recognize the fact that an air ambulance service is as necessary for our wounded as the ambulance car itself, the long haul to Tunis by the 8th and 1st Armies, with the medical answers found to most of the problems, make most interesting reading.

From page 381 to the end of the volume on page 526 much wisdom gained by experience is incorporated, forming a useful guide to the "do's" and "don'ts" of medical practice in wartime. Once again, perhaps, the maps are the one weak point in this large volume of excellently written English prose, so full of factual details well put together and documented.

J. C. A. DOWSE.

OLD WORLD SYMPHONY

Humanistic Psychology. By John Cohen. (Pp. 206. 18s.) London: George Allen and Unwin, Ltd. 1958.

Many people to-day fear that the almost explosive advance of mechanistically inclined science must bring about a desiccation and ultimate disruption of human nature. Others claim that human nature necessarily transcends all mechanistic conception, and science is therefore in the long-run nugatory. Some, with more sincerity than logic, seem to entertain both notions simultaneously. Professor Cohen is firmly convinced of the error of many of his fellow-psychologists' mechanical ways, though whether this error is intellectual or moral he does not make entirely clear. In this book he takes up the challenge and seeks to infuse his subject with something of a leisured contemplative culture. Some readers will find this soothing; others may feel that the force of his intentions has run away with his good judgment and taste. The book incorporates a lot of rather inconclusive lines of psychological discussion, and clear purpose seems to yield to face value. There is a plethora of ornament in the shape of literary allusions and quotations; these are richly varied and culturally U, but not always telling. The general effect of all this is rather forcibly reminiscent of an architectural exercise in the false-antique.

Where the text comes within brushing distance of the humdrum concerns of science it is apt to become puzzling. In a chapter on "Work and Play," for example, we start with the time when "'work' was only of interest to astronomers and . . . was expressed mathematically as the product of celestial distance and celestial force," so that "the notion of astronomical 'work' done by planets when falling through a certain distance was sufficient for an age of navigation." Within four pages the discussion has moved via, *inter alia*, Virgil's *Georgics* to reach St. Thomas Aquinas, but not without stirring up again old confusions, now sufficiently resolved, about the use of the word "work" in various scientific contexts. And the neurologist and psychiatrist may find some of the statements made in the chapter on the psychological meaning of illness interesting but steep.

Are Professor Cohen's quixotic flourishes really necessary? The ordinary scientist concerned with human nature, preoccupied as he may be with the possibilities of mechanistic interpretation, does not always fail to appreciate and practise humanity. As to Humanism at large, surely it lives only through constant re-creation by the encounter between fresh discovery and prevailing human impulse and tradition? A pot-pourri of old tunes, however sweet and skilful, is no substitute for a new symphony.

R. C. OLDFIELD.

CHEST AND LIMB LEADS

Die Neuzeitlichen Brustwand- und Extremitäten-Ableitungen in der Praxis. By Herbert Reindell and Helmuth Klepzig. Foreword by Ludwig Heilmeyer. Third edition. (Pp. 192 +viii; illustrated. DM 29.50.) Stuttgart: Georg Thieme. Verlag. 1958.

This book on modern chest and limb leads in practice should have better illustrations if the reader is to see them clearly. Many are marred by alternating current; in many instances the complexes of various leads overlap one another and so are hard to distinguish. The time-marking and the labelling of deflections are far from clear in numerous examples. The diagram of the effect of infarcts on the vector loop might be larger and so easier to see. The captions are clear and full. The letterpress is well set out and gives the theories of the electrocardiogram very well. The discussion of infarction is excellent. There are many references.

TERENCE EAST.

A group of scientists have collaborated in the production of *Space Research and Exploration* (Eyre and Spottiswoode, Ltd.; 25s.). The book, which is published under the editorship of Professor D. R. Bates, gives a general survey of the whole field of astronautics, and includes a chapter on medical and biological problems by Dr. A. E. Slater.

The *Transactions of the American Goiter Association 1956* contains 38 papers presented at the annual session of that association in Chicago, 1956. It is available in this country from Blackwell Scientific Publications, Ltd., Oxford (473 pages; £6 6s.).

A monograph on *South African Snake Venoms and Antivenoms*, by P. A. Christensen, has been published by the South African Institute for Medical Research, P.O. Box 1038, Johannesburg. There are about fifty species of venomous snakes in South Africa and the author has attempted to bring together all the available information on their venoms and antivenoms. A bibliography of over 350 references is included.

The *Cumulative Supplement 1957* to the *British Encyclopaedia of Medical Practice* (Butterworth and Co.; 35s.) provides information on matters where current practice or knowledge differs from that given in the main volumes of the *Encyclopaedia*. Subjects are arranged in the same order as in the original volumes; adequate references to the literature are provided. Issues of the *Supplement* are cumulative, so that only the latest one issued need be consulted. *Medical Progress* (Butterworth and Co.; 37s. 6d.), an annual volume complementary to the *Encyclopaedia*, gives an account of all forms of medical research published during the year, whether established or not. The volume for 1957 contains critical surveys of ten medical and surgical specialties, an account of recent developments in pharmacology and therapeutics, and abstracts of recent papers. The combined price for the *Cumulative Supplement* and *Medical Progress* is 67s. 6d.

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A PROUD RECORD

Jubilees, centenaries, and other historical commemorations might, if they directed attention merely to the beginnings of great developments and the inevitable contrast with present achievements, tempt us to complacency as well as just pride. There is certainly cause for pride in looking back on the story of the Royal Army Medical Corps,[1] which celebrates next week its Diamond Jubilee, but inspiration rather than complacency is the keynote of its record, which is one of enterprise (both corporate and individual) and courage. Set in its wider historical background, where the Corps has grown to full maturity in the ordeal of two world wars and in a century which must be regarded as one of the great watersheds of history, this one organization has made a significant contribution to events which have transformed the lives of millions.

From unpromising beginnings in the closing years of Queen Victoria's reign, when only the long-fought campaign of the medical profession, organized and led by the B.M.A., brought order and the opportunity for better things to an army medical service which was disintegrating and threatened with complete breakdown, the R.A.M.C. has become an indispensable part of British medicine. The opportunities, which have often been hedged about with all kinds of difficulties, have been readily and firmly seized by a succession of gifted administrators, the foundations being well and truly laid by Sir Alfred Keogh during the first decade of the century. Responsive to every challenge of war, individual officers who have refused to become captives to bureaucracy have made possible great advances, in scientific knowledge as well as in organization, through a series of brilliant improvisations. Elsewhere in this issue (p. 1472) a correspondent recalls some phases in the careers of "soldier doctors" of distinction. The combination of efficient organization and individual enterprise found in the R.A.M.C. has produced results which would have seemed beyond the wildest dreams of those who, on June 23, 1898, when the Royal Charter was signed, looked only for a new chapter in an old story. Few of them could have foreseen the powerful influence which the new Corps would one day exert. For over a third of its history conscription has been in force, and few able-bodied citizens have not experienced the medical care available to the armed Forces. The general standard of hygiene in Britain must have been much improved over the years by the assiduous instruction carried on by officers of the Corps among millions of serving soldiers. In pursuing its chief aim—the preservation of health—the R.A.M.C. has been active on all fronts, and its officers have themselves made important original contributions to medical and surgical knowledge.

Already, before the first war, the work of Bruce on undulant fever and, with others on the Sleeping Sickness Commission, on trypanosomiasis, together with Leishman's discovery of the protozoon responsible for what had been called "Dum-dum fever" (leishmaniasis), had shown that scientific work of the highest order could be carried out under the aegis of the Corps. The success of immunization against the enteric group of infections during the first world war, developed from the work of Almroth Wright, will always rank as one of the triumphs of army medicine, and the investigations carried out at the Royal Army Medical College on the value of selected virulent typhoid strains in vaccine production were of great immunological significance. Another remarkable achievement in preventive medicine has been the Army scheme of tetanus immunization. Even at a time of general restriction, when the size of the Corps was drastically, and some think dangerously, reduced, notable scientific work continued. In India, for instance, J. S. K. Boyd's studies of dysentery bacilli placed on a firm basis our knowledge of the antigenic structure of this group of organisms. The facilities available in the R.A.M.C. for extensive epidemiological surveys, statistical studies, and clinical trials were widely and skilfully used during the second world war and set the pattern for later work of this kind. Hamilton Fairley's large-scale trials of antimalarials at Cairns will always hold its place in the annals of tropical medicine, and it was on the field of battle that penicillin began a new era in therapeutics. Many of the great advances in modern surgery have developed from knowledge gained in the two wars. The Army Blood Transfusion service, brilliantly organized by the late Sir Lionel Whitby, has been the model for the national service which has already saved countless lives. These are but a few of the many achievements of the R.A.M.C., and are, no doubt, the precedents

[1] *See* P. Lovegrove, *Not Least in the Crusade. A Short History of the Royal Army Medical Corps*, 1951, Aldershot. For an account of the scientific work of the R.A.M.C., see *J. roy. Army med. Cps*, 1948, **90**, No. 6 (Jubilee Number).

for many yet to come. With its own College, established in its buildings at Millbank in 1907, recognized as a school for postgraduate teaching and research in the University of London, its own scientific journal (founded in 1903), its own hospitals and nursing service, it has a high place among medical institutions, not only in Britain but throughout the world.

LEUCOCYTE ANTIBODIES

The realization that many cases of acquired haemolytic anaemia appear to be brought about by the action of anti-red-cell antibodies has led to a search for analogous antibodies against platelets in thrombocytopenic purpura and against leucocytes in various types of granulocytopenia. Anti-platelet and anti-leucocyte antibodies in fact appear to be of considerable clinical importance. However, the detection of the antigens or antibodies is not as easy as with red cells, one reason being the tendency of the platelets and leucocytes to undergo spontaneous clumping. The techniques are still in the experimental stage and so far have been rarely used outside specialized laboratories. Here there is only space to mention some recent work on leucocyte antibodies, but the subject already has a large literature; J. Dausset,[1] in a recent editorial, lists 79 references, almost all published since 1952.

First of all, what are the essential facts about leucocyte antigens? According to B. W. Gurner and R. R. A. Coombs,[2] who used the technique of "mixed erythrocyte–leucocyte agglutination," A and B and MN type antigens are present but not the Rh antigens. In these respects leucocytes resemble platelets. In addition to these antigens, which leucocytes share with red cells, it seems probable that a complicated system of leucocyte groups, distinct from the red-cell groups, exist. The basis for this conception is that sera containing leucocyte agglutinins differ in their capacity to cause the agglutination of apparently compatible leucocytes. For example, Dausset[3] lists the results obtained with 19 sera tested with between 32 and 178 different samples of human leucocytes. The sera agglutinated between 55% and 100% of the leucocytes tested. In addition to these surface antigens, nuclear and cytoplasmic antigens apparently exist.[1]

The circumstances in which leucocyte agglutinins are found in human sera has been the subject of several large surveys. Most authors[4 5] have used an agglutination test the basis of which is the suspension of normal compatible leucocytes in heat-inactivated patient's serum. In this way R. Payne[5] found agglutinins in the serum of 38 out of 350 patients with various blood diseases. Fifty sera from healthy medical students were free from agglutinins. The majority of the patients were not leucopenic at the time of testing. Thirty-four of the patients whose sera contained agglutinins had been transfused, and there appeared to be an increasing tendency for the tests to be positive as the number of transfusions increased. The antibodies in the four sera from patients who had not been transfused were weak and inconstant. Payne concluded that the antibodies she was dealing with were iso-antibodies provoked by previous transfusion; in this she was supporting the conclusion of earlier workers.[4] Only one-third of the patients whose sera contained leucocyte agglutinins had leucopenia, and Payne lists arguments against the hypothesis that leucocyte antibodies are responsible for certain cases of "idiopathic" leucopenia ("immunoleucopenia"); in particular, she cites the fact that the leucocyte agglutinins have failed almost invariably, when tested, to cause convincing agglutination of the subject's own leucocytes.

More recently J. L. Tullis[6] has published the results of a survey of the incidence of leucocyte antibodies in a variety of pathological states. He used an index based on an assessment, following one hour's incubation at 37° C., in a mixture of the test serum and complement, of the leucocyte loss by clumping or lysis, and also of their loss of mobility. He studied 132 sera from leucopenic patients and 102 sera from patients without leucopenia; 70 positive results were obtained, but, contrary to Payne's observations, the majority (59 out of the 70) were given by the sera of leucopenic patients. Most of these patients were classified as having primary agranulocytosis, or primary or secondary hypersplenism. Tullis stresses that positive results are not usually obtained in leucopenia associated with aplasia of bone marrow. Again, contrary to the generally accepted view,[5 7] he regards the development of iso-agglutinins in the leucopenic cases as indicating that the leucopenia is in reality of auto-antibody origin, and he records several cases in which clinical improvement was associated with the disappearance of anti-leucocyte activity.

Dausset[1] summarizes present views on the existence of auto-antibodies against leucocytes as follows: there is good evidence for their presence in disseminated lupus erythematosus; in the leucopenias and "idiopathic" agranulocytosis the role of antibodies is controversial, as is the presence of leuco-precipitins

[1] Dausset, J., *Vox Sang. (Basel)*, 1957, **2**, 225.
[2] Gurner, B. W., and Coombs, R. R. A., ibid., 1958, **3**, 13.
[3] Dausset, J., Malinvand, G., and Brécy, H., *Immuno-Hématologie Biologique et Clinique*, 1956, Paris, E.M.F.
[4] —— Nenna, A., and Brecy, H., *Blood*, 1954, **9**, 696.
[5] Payne, R., *Arch. intern. Med.*, 1957, **99**, 587.
[6] Tullis, J. L., *New Engl. J. Med.*, 1958, **258**, 569.
[7] Walford, R. L., Peterson, E. T., and Doyle, P., *Blood*, 1957, **12**, 953.
[8] Payne, R., *Vox Sang. (Basel)*, 1957, **2**, 233.

in acute leukaemia; and in agranulocytosis due to drug sensitivity, though it is logical to suppose that an antibody mechanism may operate, the presence of an antibody in the patient's serum capable of causing agglutination in the presence of the drug has not been convincingly shown. He mentions, however, the possibility that the failure to find auto-antibodies in granulocytopenia and agranulocytosis could be explained by the antibody existing in an incomplete form not readily detected by direct agglutination tests.

Although it is clear that the role of auto-antibodies against leucocytes has not yet been satisfactorily established, iso-antibodies certainly exist and are clinically important in at least one respect. Payne,[8] in a recent paper, summarizes previous observations which suggested that patients whose sera contained leucocyte agglutinins were particularly prone to develop febrile transfusion reactions and reports her own extensive data. Leucocyte agglutinins were found to be present in the sera of 32 out of 49 patients reported as having unexplained febrile reactions to transfusion. All the patients giving positive tests had been transfused, while in thirteen of fifteen closely studied patients receiving repeated transfusions the first discovery of leucocyte agglutinins coincided with the first onset of a febrile reaction. Eleven patients whose sera contained agglutinins and who had experienced febrile reactions were transfused with "leucocyte-free" (washed) blood containing less than 200 leucocytes per c.mm. No reactions resulted.

NEOMYCIN IN OPHTHALMOLOGY

The use of antibiotics in ophthalmology can be divided into three categories: first, the treatment of infections of the soft tissues around the eye, as for example orbital cellulitis; second, the treatment of surface infections such as blepharo-conjunctivitis; and third, the treatment of deep corneal ulceration and endophthalmitis where the globe itself is involved.

The treatment of paraocular cellulitis is by systemic administration of antibiotics and differs in no way from the treatment of cellulitis elsewhere. Superficial infections can usually be dealt with by the topical application of antibiotic drops or ointment. The treatment of infections of the eye itself, however, presents special difficulties, since neither by topical application nor by systemic administration do antibiotics enter the intraocular fluids in sufficient quantity to be of therapeutic value. Only by subconjunctival injection of a concentrated antibiotic solution can satisfactory intraocular levels be attained. To be suitable for subconjunctival injection an antibiotic must be highly soluble in water and the solution must be relatively non-irritating to the tissues. Penicillin, streptomycin, and polymyxin fulfil these conditions and can be given subconjunctivally in the treatment of ocular infection.[1-3] Chloramphenicol, chlortetracycline ("aureomycin"), oxytetracycline ("terramycin"), and erythromycin are unsuitable for subconjunctival injection, because their solubility in water is too low; tetracycline is slightly more soluble than other similar antibiotics but is not sufficiently so to be thoroughly satisfactory for subconjunctival injection.

A recent report by A. Sorsby and J. Ungar[4] indicating the suitability of neomycin for subconjunctival injection is therefore of considerable interest. Neomycin is not a new antibiotic, for its general properties were described by S. A. Waksman and H. A. Lechevalier[5] in 1949, and its value as a topical application in the treatment of superficial ocular infection is well recognized. A. W. Vogel and colleagues[6] noted that solutions of 100 mg. per ml. were well tolerated when given subconjunctivally, but gave no record of the amounts reaching the intraocular fluids. G. Lepri[7] found that a therapeutic level of neomycin was attained in the aqueous humour of the rabbit's eye one hour after the subconjunctival injection of 30 mg. of neomycin dissolved in 0.5 ml. of water containing adrenaline. Sorsby and Ungar, however, have now shown that 500 mg. of neomycin dissolved in 1 ml. of 1:4,000 adrenaline solution may be given safely by subconjunctival injection. Furthermore, one such injection produces a therapeutic level of neomycin in the aqueous humour lasting for twenty-four hours. Initial clinical trials appear to confirm that subconjunctival injections of neomycin are practicable.

It is still too early to assess the value of neomycin in comparison with other antibiotics in the treatment of intraocular infection; but, since neomycin has a very wide range of antibiotic activity and sensitive organisms do not readily develop increased resistance,[8] it seems probable that it will be very useful. Intraocular infections progress with great rapidity and early effective treatment is essential if sight is to be saved. As neomycin is active against both cocci and

[1] Sorsby, A., and Ungar, J., *Brit. J. Ophthal.*, 1947, **31**, 517.
[2] —— and Bailey, N. L., *Brit. med. J.*, 1952, **1**, 119.
[3] Ainslie, D., *Brit. J. Ophthal.*, 1953, **37**, 336.
[4] Sorsby, A., and Ungar, J., *Ann. roy. Coll. Surg. Engl.*, 1958, **22**, 107.
[5] Waksman, S. A., and Lechevalier, H. A., *Science*, 1949, **109**, 305.
[6] Vogel, A. W., Leopold, I. H., and Nichols, A., *Amer. J. Ophthal.*, 1951, **34**, 1357.
[7] Lepri, G., *Rass. ital. Ottal.*, 1952, **21**, 419.
[8] Lopez, S. P., *Antibiot. and Chemother.*, 1954, **4**, 1189.

Gram-negative bacilli it may well prove invaluable when the nature of the infecting organism is not immediately apparent.

X RAYS AND THYROID CANCER

In 1950 workers at the Memorial Hospital in New York reported[1] that 10 of 28 children under the age of 15 with proved thyroid cancer had received *x*-ray therapy to the thymus gland in infancy. The authors suggested there might be a greater risk of cancer developing after *x*-ray therapy given to children. There were no further published reports of a possible association between *x* rays and thyroid cancer until 1955, when a follow-up study[2] of 1,722 children who had received *x*-ray therapy for enlarged thymus showed a greater frequency of thyroid cancer and other tumours in these children than in their 1,933 siblings who had not received *x*-ray therapy. C. L. Simpson and colleagues[3] have recently published further data on these children. With 87% of the treated group traced, they have found 10 thyroid cancers in the *x*-ray-treated children and none in their untreated siblings. "The expected number of cases of thyroid cancer in the treated group was 0.06," so the observed figure would appear to be highly significant. The average latent period between *x*-ray therapy and the development of thyroid cancer was 12.1 years, and the skin *x*-ray dose was between 240 and 1,400 r.

The carcinogenic effect of *x* rays is known to be potentiated by a number of factors (infective, chemical, hormonal).[4] I. Doniach[5] has reported that thyroid cancer developed in 5 rats out of 24 given 30 microcuries of iodine-131 followed by prolonged administration of methylthiouracil. Seven of 21 rats treated with 1,100 rads of *x* rays to the thyroid and methylthiouracil developed thyroid cancer. There was one thyroid cancer in the group given *x* rays without added goitrogen. No cancers were observed in the rats given either iodine-131 or methylthiouracil alone during the period of observation. Doniach[6] suggests that the carcinogenic action of small doses of *x* rays to the infant thyroid may be promoted by the stimulus afforded by the normal growth and development of the thyroid gland. This occurs from birth to puberty and is analogous to the experimental treatment with goitrogen.

A recent review[7] of this subject suggests that diagnostic and test doses of iodine-131 should be restricted in the pre-adolescent patient, because of the clinical and laboratory evidence of increased risk of development of thyroid cancer after relatively small doses of *x* rays to children. The administration to children of thyroid extract following iodine-131 treatment would tend to minimize any increased pituitary activity, which, experimentally at least, increases the number and malignancy of thyroid tumours after ionizing radiation.

[1] Duffy, B. J., and Fitzgerald, P. J., *Cancer*, 1950, **3**, 1018.
[2] Simpson, C. L., Hempelmann, L. H., and Fuller, L. M., *Radiology*, 1955, **64**, 840.
[3] —— —— *Cancer*, 1957, **10**, 42.
[4] Furth, J., and Lorenz, E., in Hollaender, A., Ed., *Radiation Biology*, 1954, **1**, 1145. New York.
[5] Doniach, I., *Brit. J. Cancer*, 1957, **11**, 67.
[6] —— ibid., 1957, **11**, 253.
[7] Duffy, B. J., *J. clin. Endocr.*, 1957, **17**, 1383.

NAMING OF HAEMOGLOBINS

For nearly 100 years only two human haemoglobins were known—adult haemoglobin (A) and foetal haemoglobin (F). Ten years ago H. Hörlein and G. Weber[1] noted that the abnormal spectrum of a methaemoglobin found in a family with familial methaemoglobinaemia was associated with the globin part of the molecule. This familial abnormal methaemoglobin was later called haemoglobin M.[2] Following the fundamental discovery by L. Pauling and his associates[3] that sickle-cell anaemia is caused by an abnormal haemoglobin (haemoglobin S) many other variants of adult haemoglobin have been discovered. In 1953 a group of interested workers in the United States met under the chairmanship of Professor J. V. Neel to decide on a standard system of nomenclature.[4] The letters A, F, and S were then retained as the designations for adult, foetal, and sickle-cell haemoglobin owing to their mnemonic associations. The other haemoglobins were assigned letters of the alphabet in order of their discovery beginning with the letter C (since B or b had at one time been used for the sickle-cell haemoglobin). Later the letter M was given to the abnormal methaemoglobin of Hörlein and Weber. Thus in addition to the "mnemonic" haemoglobins A, F, S, and M we now have haemoglobins C, D, E, G, H, I, J, K, L, N, O, and Q. Haemoglobin O is described by its discoverer, Lie-Injo Luan Eng, at p. 1461 of the *Journal* this week. P has been claimed for the Galveston type described by R. G. Schneider and M. E. Haggard[5] prior to haemoglobin Q. At present such haemoglobins not yet named include Hopkins I and Hopkins II,[6] and two possibly abnormal foetal haemoglobins, one a nameless pigment described by P. Fessas and A. Papaspyrou[7] and the Bart's haemoglobin of J. A. M. Ager and H. Lehmann.[8] Doubtless other new haemoglobins are in the process of being detected, and some now thought to be identical by present-day techniques may turn out to be different.

With the increasing number of haemoglobins described there is a real need for some permanent central organization to prevent confusion in naming them. When the American workers met in 1953 to devise the current method of nomenclature they could not have foreseen how many of these haemoglobin variants were about to be discovered and how quickly publications were to follow one another. A cautionary example of the muddle that can occur is given by the history of a new haemoglobin found by R. Cabannes

[1] Hörlein, H., and Weber, G., *Dtsch. med. Wschr.*, 1948, **73**, 476.
[2] Singer, K., *Amer. J. Med.*, 1955, **18**, 633.
[3] Pauling, L., Itano, H. A., Singer, S. J., and Wells, I. C., *Science*, 1949, **110**, 543.
[4] *Blood*, 1953, **8**, 386.
[5] Schneider, R. G., and Haggard, M. E., *Nature (Lond.)*, 1957, **180**, 1486.
[6] Smith E. W., and Torbert, J. V., *Bull. Johns Hopk. Hosp.*, 1958, **102**, 38.
[7] Fessas, P., and Papaspyrou, A., *Science*, 1957, **126**, 1119.
[8] Ager, J. A. M., and Lehmann, H., *Brit. med. J.*, 1958, **1**, 929.
[9] Cabannes, R., and Buhr, L., *Pediatrie*, 1955, **10**, 888.
[10] Rucknagel, D. L., Page, E. B., and Jensen, W. N., *Blood*, 1955, **10**, 999.
[11] Jensen, W. N., Page, E. B., and Rucknagel, D. L., *Clin. Res. Proc.*, 1955, **3**, 93.
[12] Rigas, D. A., Koler, R. D., and Osgood, E. E., *Science*, 1955, **121**, 372.
[13] Cabannes, R., Duzer, A., Portier, A., Massonhat, J., Sendra, L., and Buhr, J. L., *Sang*, 1956, **27**, 580.
[14] Thorup, O. A., Itano, H. A., Wheby, M., and Leavell, B. S., *Science*, 1956, **123**, 889.
[15] Lehmann, H., *Blood*, 1957, **12**, 90.
[16] *Brit. med. J.*, 1958, **1**, 1170.
[17] Neel, J. V., *Ann. hum. Genet.*, 1956, **21**, 1.
[18] Malassenet, *Rev. Hémat.*, 1957, **12**, 64.
[19] *Brit. med. J.*, 1957, **1**, 1235.

and L. Buhr in 1955,[9] and called by them I. Unknown to the Algerian workers the letter I had by then been allotted by D. L. Rucknagel and colleagues[10] to a haemoglobin which they had originally named H,[11] not being aware at the time that the letter H had been given to a newly discovered haemoglobin by D. A. Rigas and colleagues.[12] Cabannes and his team[13] altered their designation from I to J, but then found that this letter had been given to a new haemoglobin by O. A. Thorup and others.[14] At the end it was decided at the Sixth Congress of the International Society for Haematology in Boston to rename this haemoglobin for a third time and it has since been known as haemoglobin K.[15]

In time it may be possible to give chemical definitions of haemoglobins based on the analysis of the globin protein chains. V. M. Ingram's work showing that haemoglobins A, S, and C differ by one amino-acid, discussed recently in these columns,[16] points to one way in which this might become possible. At any rate, the increasing number of haemoglobins necessitates for their identification a variety of techniques of which some are more complex than others, and not every laboratory can expect to have at its disposal reference samples of all the known haemoglobins. Either a closely knit system of national reference laboratories or an international reference laboratory is thus likely to be necessary if confusion is to be avoided. The task of such a laboratory would in the first place be to identify specimens. A second task, perhaps not quite as essential, would be for it to act as a collection and distribution centre for authenticated samples of rare haemoglobins for research purposes. It could be of help in the study not only of human haemoglobins but of the various animal haemoglobins too. The need for some such organization has been expressed elsewhere.[17 18] Meanwhile in Britain there exists under the chairmanship of Professor A. W. Woodruff, of the London School of Hygiene and Tropical Medicine, a working party on sickle-cell anaemia and sickle-cell trait which advises the Medical Research Council and the Colonial Medical Research Committee. It is carefully considering these problems, and has already recommended a nomenclature for the clinical haemoglobin states[19] which has found wide acceptance.

PEPTIC ULCER IN TWINS

If monozygous twins, with their identical genetic constitution, are more often both affected with a particular disease than are dizygous twins, this provides preliminary evidence that genetic factors are important in causing the disease. Two main reservations have been suggested to taking the findings in twins at their face value. One is that monozygous twins have a special psychological relationship which may lead them into similar experiences more often than dizygous twins; the other is that monozygous twins, when they have a common chorion, may suffer circulatory disturbances *in utero*, providing an environmental cause of differences to which dizygous twins are not subject. These reservations will be important for some characters under study but much less for others. The major practical difficulty in twin study is to secure a sufficiently large and unbiased sample of monozygous and dizygous twins. For example, B. Simonds[1] found, when asking colleagues to refer to her patients from chest clinics who were one of a twin pair, that she was notified of disproportionately many monozygous pairs. To get an unbiased sample she found it necessary to write personally to a large series of patients asking each of them if they had a twin. Patients tend to volunteer information that they are one of a twin pair more often if the twin is monozygous.

It has been known for some time that there is a tendency for peptic ulcer to show a concentration in families, and some striking individual pedigrees are on record.[2] The best systematic study of families with peptic ulcer was that of R. Doll and J. Buch,[3] who, having determined the incidence of peptic ulcer in a North London population, were able to show that the incidence in first-degree relations of peptic-ulcer patients in the same area was notably raised. They further noted that the ulcer in a relation tended to be of the same type, duodenal or gastric, as in the index case. Such family concentration is not necessarily due to genetic resemblance: common family environment is an alternative explanation. With twin comparisons, however, the common family environment will, with the reservations mentioned above, apply to both types of twins. Now two recent twin studies, one Danish[4] and one Australian,[5] have given some support to the view that genetic factors play their part in causing peptic ulcer. The Danish series was collected as part of a follow-up of all twins born in Denmark between 1870 and 1910. It is recorded that 6 of 23 monozygous co-twins and 5 of 41 dizygous co-twins of the same sex were each found to be also affected with peptic ulcer. With this method of ascertainment the findings give concordance rates of 12 in 29 for monozygous pairs and 10 in 46 for dizygous pairs. The Australian series was of 20 patients attending a Melbourne hospital, each of whom had duodenal ulcer and was a member of a twin pair. In 8 instances the patient or the co-twin was dead, and in 2 further instances it was not possible to examine the co-twin. The 10 remaining patients were all male. In 2 instances only was the co-twin monozygous; one of these also had proved duodenal ulcer, the other was also probably affected, since he had had indigestion for many years and was found to have scarring of the duodenal cap on radiography. Of the 3 male dizygous twins 2 were free of symptoms, while the other had had one attack of melaena and also indigestion for many years and was probably affected. These two series are too small to be of much significance statistically, but the differences are in the direction of higher concordance for the monozygous pairs.

[1] Simonds, B., *Eugen. Rev.*, 1957, **49**, 25.
[2] Wright, J. T., Grant, A., and Jennings, D., *Lancet*, 1955, **2**, 1314.
[3] Doll, R., and Buch, J., *Ann. Eugen. (Camb.)*, 1950, **15**, 135.
[4] Harvald, B., and Hauge, B., *Dan. med. Bull.*, 1956, **3**, 150.
[5] Doig, R. K., *Med. J. Aust.*, 1957, **2**, 617.
[6] Aird, I., Bentall, H. H., Menigan, J. A., and Roberts, J. A. F., *Brit. med. J.*, 1954, **2**, 315.
[7] Clarke, C. A., Wyn Edwards, J., Haddock, D. R. W., Howel-Evans, A. W., McConnell, R. B., and Sheppard, P. M., ibid., 1956, **2**, 725.

It is clear that some of the genetic factors in the causation of duodenal ulcer will be linked with the relationship of the ABO groups and secretor status with duodenal ulcer.[6,7] Members of the same family, including dizygous pairs, will resemble each other more often than unrelated persons in their ABO and secretor status, while monozygous twins will be identical for these characters. It will be instructive in later twin studies to distinguish between those dizygous pairs who are like and those who are unlike for blood group and secretor status. It is possible that those dizygous pairs who are the same for these characters will prove as often concordant for duodenal ulcer as are monozygous pairs. On the other hand, if this proves not to be the case, it will suggest that there are genetic factors predisposing to ulcer formation in addition to those determining the ABO group and secretor status.

TALC AND PERICARDIAL CALCIFICATION

Inhalation of talc as a cause of pericardial calcification has recently been suggested by M. Kleinfeld and C. P. Giel.[1] In a review of 37 workers employed for long periods in talc mills or mines, they found pericardial calcification, as a chance radiological observation, in three patients, whose ages were 64, 68, and 79 years. The evidence that inhalation of talc was responsible for pericardial calcification was indirect, since none of the three patients came to necropsy. The long history of exposure to talc—namely, 24, 34, and 47 years—coupled with radiographic evidence of talc pneumoconiosis, with pulmonary infiltration and pleural and diaphragmatic calcification, suggested the possibility that the pericardial calcification might also be due to talc. In addition, the incidence of pericardial calcification in the group of talc workers studied was very much higher than could be explained by chance. None of the three patients had evidence of constrictive pericarditis and none showed any abnormality in the electrocardiogram.

Symptomless pericardial calcification is well recognized.[2] It may occur either with a normal electrocardiogram or with an abnormal one, which itself may have led to a careful search for evidence of past pericarditis in the form of calcification in the radiograph of the chest. Inhalation of talc, therefore, may now be added as another possible cause of this finding, especially if there is evidence of pulmonary infiltration, with calcification of the pleura and diaphragm.

The difference between symptomless pericardial calcification and calcific constrictive pericarditis is probably only one of degree, and the main interest of this report lies in the possibility that inhalation of talc may rarely be the cause of constrictive pericarditis, though no evidence of constriction was seen in the present study. The commonest cause of constrictive pericarditis is without question tuberculosis,[3] but there remain a few patients in whom the cause is obscure. Some of these cases may be due to old pyogenic pericarditis and others to trauma and a haemopericardium. It is possible, however, that a few may be due to inhalation of some irritant, such as talc, particularly if there is associated lung disease.

[1] Kleinfeld, M., and Giel, C. P., *Monthly Review*, Division of Industrial Hygiene, N.Y., 1957, **36**, 33.
[2] Mathewson, F. A. L., *Circulation*, 1955, **12**, 44.
Evans, W., and Jackson, F., *Brit. Heart J.*, 1952, **14**, 53.

BIRTHDAY HONOURS

The award of the Order of Merit to Sir Macfarlane Burnet, F.R.S., in the Birthday Honours is a fitting tribute to this distinguished medical investigator. As director of the Walter and Eliza Hall Institute at Melbourne, Sir Macfarlane has long held an international reputation for his virus researches, particularly those on the influenza virus. But he has often ranged far beyond the detailed laboratory study of these organisms to throw light on the wider problems of immunity, malignant growth, and genetics. The *Journal* was privileged to publish an impressive contribution of this nature a year ago.[1] There Sir Macfarlane classified himself as one of those scientists "who believe that at every stage in scientific development it is necessary to provide the best available generalizations as a guide to effective work, both in the application of knowledge to human needs and in the planning of human research." In this role, which only a few are gifted enough to fill successfully, Sir Macfarlane has won the same pre-eminence as in his studies of virus genetics.

The great contributions of medical men in the Antipodes to the advancement of medicine are recognized in this honours list, five knighthoods being awarded to Australians and New Zealanders. Professor J. C. Eccles, F.R.S., is a distinguished neurophysiologist whose main researches have been concentrated on the transmission of the nervous impulse. As a Rhodes scholar at Oxford he was a pupil of Sherrington's; since 1951 he has been professor of physiology at the Australian National University, Canberra. Two well-known surgeons who receive knighthoods are Mr. B. T. Edye, of Sydney, and Mr. K. B. Fraser, of Brisbane. In New Zealand the K.B.E. is conferred on Dr. C. R. Burns, of Wellington, a leading consultant physician, and on Professor F. H. Smirk, of Otago, Lancashire-born but New Zealander by adoption, who has carried out much important research into the treatment of hypertension.

In Great Britain, Mr. J. D. McLaggan, the distinguished E.N.T. surgeon and aurist to the Queen, is advanced in the Royal Victorian Order to K.C.V.O. Brigadier J. S. K. Boyd, F.R.S., receives a knighthood. His work on the dysentery bacilli between the two world wars made him an international authority on the subject, and he has contributed in many ways to the advancement of knowledge of tropical diseases. Mr. E. W. Riches, of the Middlesex Hospital, London, one of the leading urological surgeons in the world, receives a knighthood. A Canadian medical man, Dr. A. G. Curphey, is knighted for public services in Jamaica, which include the presidency of the Legislative Council.

Many readers will especially welcome the award of the C.B. to Dr. G. E. Godber, Deputy Chief Medical Officer, Ministry of Health.

We record with regret the death on June 15 of Sir Arnold Stott, consulting physician to the Westminster Hospital.

[1] Burnet, M., *Brit. med. J.*, 1957, **1**, 780, 841.

DIAMOND JUBILEE OF THE R.A.M.C.

THE ARMY DOCTOR'S TWO PROFESSIONS

Sixty years ago, on June 23, 1898, Queen Victoria, then in her eightieth year, added her forthright signature to the top right-hand corner of the Royal Warrant which brought the Royal Army Medical Corps into being. The Warrant began:

"WHEREAS We have deemed it expedient to alter in certain respects the conditions under which the officers employed upon the medical duties of Our Army are at present serving:

"OUR WILL AND PLEASURE is that the officers below the rank of surgeon-major-general serving in Our Army Medical Staff shall be formed into a corps, together with the warrant officers, non-commissioned officers and men of Our Medical Staff Corps;

"IT IS OUR FURTHER WILL AND PLEASURE that the designation 'Medical Staff Corps' shall be abolished, and that the corps formed as above-mentioned shall be styled 'The Royal Army Medical Corps.'

"The following alterations will consequently be made . . ."

On that same summer's day down at Netley the company officer of Nos. 4 and 5 Companies had probably spent a busy morning handing out minor punishments to erring young soldiers, inspecting barrack rooms, arranging cricket matches, and carrying out the daily regimental chores which fall to the lot of a company officer. The officer in question was William Boog Leishman. A year or so later we find him still at Netley working with Almroth Wright in their historic battle with the typhoid bacillus.

This young officer, whose name is for ever commemorated in the nomenclature of tropical medicine and who later became both a Fellow of the Royal Society and Director-General of the Army Medical Services, aptly personifies the army doctor the British Medical Association envisaged in the report of its Parliamentary Bills Committee of 1897: "Army medical officers must be something more than doctors, must not entirely cure diseases but prevent them, not merely professionally aid the wounded but take military charge . . ."

This sentiment has since been often expressed in authoritative circles outside the medical profession. In *The Times* of August 10, 1951, for instance, we find it stated in a leading article that "Army doctors belong to two professions and unless they have mastered both they fail in their duty." Yet, in spite of the evidence of history, the belief that a soldier cannot be a good doctor, or a doctor an efficient soldier, dies hard.

Famous Soldier-Doctors

Of the famous soldier-doctors of the last sixty years Leishman has already been mentioned. The name of David Bruce, immortalized in *Brucella melitensis*, at once springs to mind. Perhaps an even greater contribution to medicine was his work in Uganda on sleeping sickness, where he described the part of *Glossina palpalis* in spreading that disease. Bruce was greatly helped in this work by Lieutenant Forbes Tulloch, a young regular officer of great charm and exceptional brilliance. Tulloch had a dazzling future before him when in 1906, at the age of 27, he unhappily succumbed to the disease he was investigating. Coming to more modern times we recall that it was W. P. MacArthur who first described the relationship of cysticercosis to epilepsy. Sir William's reputation as a physician and lecturer is well known, but a younger generation may not realize that it was his determination and initiative as Director-General which resulted in the Medical Service entering Hitler's war with an organization and equipment unsurpassed in any other branch of the Army.

If this is the time to praise famous men of the last sixty years, foremost among them must be put Sir Alfred Keogh, who as Director-General built up the Corps between 1904 and 1910 and was recalled to that post in 1914. It was under his administration that the Corps, originally designed to serve seven divisions, within four years was expanded to undertake the medical care of some five million men. Some twenty years later the hour again produced the man, and we find Sir Alexander Hood carrying into full effect a policy advocated by Sir Anthony Bowlby in the first world war. This policy largely did away with the cumbersome "line of evacuation" which damned a patient to an unhappy journey of perhaps fifty miles or more before he obtained the services of specialists congregated in hospitals at the base. Sir Alexander put the Corps on wheels, so that in the second world war specialists with their small, highly trained teams were to be found setting out across the desert to bring expert treatment to the wounded in the forward areas.

It must not be thought, however, that the Corps's diamond jubilee is just an affair of the Regulars. The

Major-General Sir David Bruce, K.C.B., F.R.C.P., F.R.S. (1855-1931). Commandant, R.A.M.C. College, Millbank, 1914-19; Assistant Professor of Pathology, Army Medical School, Netley, 1889-94.

Medical Service must always depend on the part-time soldier, and foremost among these are the Territorials. Their zeal has always been a thing to marvel at. Noel Chavasse, who won the Victoria Cross twice over, was a Territorial. After a brilliant university and hospital career, he died in 1917 of wounds received in winning his second Cross. Sir Thomas Fairbank was for many years transport officer in a Territorial field ambulance and went to France in 1915 in that capacity. He would spend his day among his transport in the Ypres salient; when his animals had been watered and fed, he would don his gown and operate far into the night. In June, 1914, an entry appeared in the *London Gazette* which must surely be unique. It read: "Lance-corporal Julian Taylor, F.R.C.S., R.A.M.C.(T.), to be lieutenant." In those days the future surgeon of University College Hospital, in spite of his F.R.C.S., bestrode a light draft-horse in an ambulance wagon.

Arthur Martin-Leake was doing a house appointment at a hospital in Hemel Hempstead when the South African war began. He at once joined the Hertfordshire Yeomanry as a trooper, later transferring to the South African Constabulary. His commanding officer, Lieutenant-Colonel Baden-Powell, induced him to transfer to the R.A.M.C. and become his regimental medical officer. Martin-Leake was grievously wounded winning the Victoria Cross, and occupied his convalescence in obtaining the fellowship of

the Royal College of Surgeons. On the outbreak of the Kaiser's war he left his appointment in India, gate-crashed in a highly unorthodox manner into France, and by November 8, 1914, as a field ambulance officer, had won a bar to his Cross. Sir Clement Price-Thomas (though it is true that he had not qualified at the time) elected to spend the first world war as an R.A.M.C. private in a field ambulance in Macedonia. Philip Mitchiner used to describe with deep feeling the arctic afternoons spent in drilling on the square at Millbank under the watchful eye of Lieutenant Webb-Johnson. He claimed to be the only man to have held every rank in the R.A.M.C. from private to major-general. Ogier Ward was a bombardier in the Honourable Artillery Company before the first world war. He was

Lieut.-General Sir William Boog Leishman, K.C.B., F.R.C.P., F.R.S. (1865–1926). Medical Director-General, Army Medical Service, 1923–6; Professor of Pathology, Royal Army Medical College, Millbank, 1903–13.

commissioned in the same regiment and spent the whole war as Gunner, winning a D.S.O. and a Military Cross and finishing as a lieutenant-colonel. Within a month or so of demobilization he had taken his fellowship and mastership of surgery and was on the staff of the professorial surgical unit at St. Bartholomew's Hospital. Other examples of distinguished soldier-doctors could be multiplied almost *ad infinitum*—Sir Lionel Whitby, a former infantry officer; Glyn Hughes, with three D.S.O.s and a Military Cross; Austin Eagger, to whom the Airborne Forces owed a great debt; and his successor, Malcolm MacEwan, another famous Territorial, who won a D.S.O. with the Gunners and a D.F.C. with the R.A.F. before joining the Corps.

Military and Civil Co-operation

One of the most striking developments in the Corps's sixty years' history has been the increase in friendly co-operation between the military and civil medical services. The South African war was largely an affair of soldiers only, and apart from awakening much patriotic fervour had little effect on the daily lives of the civil population. Hospitals were an irresistible attraction for society ladies, whose enthusiasm far outstripped their professional skill; rationing was on a more or less "Fortnum and Mason" scale. During the tragic years of 1914 to 1918 Zeppelin and other raids brought the war nearer home to the civil population, and the co-operation of the services became much closer. Most large teaching hospitals became Territorial general hospitals, but there still remained many stately homes where the lady of the manor was very much the commanding officer.

In the second world war all this was changed. Now the civil population took its full share of devastating bombardments, and *pari passu* with this came an almost complete integration of the two medical services. Abroad there was no question of special Territorial or "private enterprise" units; at home the Emergency Medical Service sprang into existence and we found Regional and Command staffs working in friendly unison, R.A.M.C. personnel of all ranks working harmoniously in E.M.S. hospitals. The old *dolce far niente* life of the convalescent depot was replaced by strenuous rehabilitation culminating in a run over a battle course.

When we contemplate the shape of things to come it may well be that a future war will bring more wholesale destruction and suffering to the civil population than to many of the troops in forward areas. In this contingency any dichotomy in the medical services would be fatal. In 1939 the Emergency Medical Service was largely in the nature of a blueprint, put into effect on the immediate threat of war with little rehearsal. To-day a far-seeing Director-General is taking no chances. Any who have seen something of the new "Support Treatment" designed to bring expert help by air wherever it is wanted in a matter of hours, or have participated in the elaborate "Exercises in aid of the Civil Power," will look forward with increasing confidence to the part the Corps would play in war which everybody hopes will never happen.

The photographs of Sir David Bruce and Sir William Leishman are reproduced from copies at the Royal Army Medical College, Millbank, by kind permission of the Commandant.

R. E. B.

BRITISH SPAS FEDERATION

HORDER MEMORIAL LECTURE

The late Lord Horder was president of the British Spas Federation for over ten years, and to commemorate the work he did in that office the Federation founded a memorial lecture which bears his name. The first memorial lecture was given by Sir Harry Platt in Droitwich, the second by Sir Russell Brain at Bath, and the third was given last week, on June 10 at the Royal Society of Medicine, by Dr. Howard Rusk, of New York. Introducing the speaker, Professor R. E. TUNBRIDGE, who succeeded Lord Horder as president of the British Spas Federation, recalled Dr. Rusk's distinguished career as an international authority on rehabilitation, mentioning that he was also an associate editor of the *New York Times*.

Dr. Howard Rusk's Address

Dr. RUSK began his lecture with some personal reminiscences of Lord Horder, describing him as one of the great leaders who had brought clinical pathology to the practice of medicine. He was also one of the first to stress the need for the patient to be taught to do things for himself—part of the process of rehabilitation. Reviewing the development of the rehabilitation services in the U.S.A. during and after the second world war, Dr. Rusk said that at the end of the war there were 2,500 paraplegics among the veterans. At the present time 1,763 of these were living in their own homes, driving their own cars, and 1,400 were in some gainful occupation. Among civilians in the U.S.A. it was estimated that there were some 12,500 paraplegics. For these disabled people there ought to be the same opportunities for rehabilitation as for the disabled veterans. There were 1,400,000 hemiplegics in the U.S.A., and here again, if the facilities were available, rehabilitation worked wonders. In a special study of 3,000 cases it had been found that 88% could be trained to meet the needs of ordinary living. There was no correlation between the degree of neurological insult and the results of treat-

ment and training. The physicians carrying out this study found that patients did well if they had someone to love them, a home to return to, and a job to go to. In his own department at the Bellevue Hospital Dr. Rusk had been getting very encouraging results in the treatment of children with spina bifida.

After describing how rehabilitation could be an international project, giving unequalled opportunities for improving relations between nations, Dr. Rusk concluded his lecture by discussing the need for "stress" as a therapeutic aid. Stress in this sense was a "purposeful, driving activity." It was having such a purpose that made people happy. Lord Horder himself was an example of this.

Proposing the vote of thanks to the speaker, Sir RUSSELL BRAIN said that the lecture was an admirable commemoration of Lord Horder, and he congratulated Dr. Rusk on the great contribution he was making to international friendship—to the rehabilitation of international relations, in fact.

After the lecture Professor R. E. Tunbridge and the British Spas Federation entertained Dr. and Mrs. Rusk and a number of other guests, including the Minister of Health, to dinner at the Royal Society of Medicine.

MEDICAL BIRTHDAY HONOURS

The names of the following members of the medical profession were included in a Birthday Honours List published in *Supplements* to the *London Gazette* on June 12.

O.M.

Sir FRANK MACFARLANE BURNET, M.D., Ph.D., Sc.D., F.R.C.P., F.R.A.C.P., F.R.S. Director, Walter and Eliza Hall Institute for Medical Research, Melbourne, and Professor of Experimental Medicine, Melbourne University. Chairman, National Radiation Advisory Committee.

K.C.V.O.

JOHN DOUGLAS MCLAGGAN, C.V.O., M.B., Ch.B., F.R.C.S., F.R.C.S.Ed. Lecturer in Diseases of the Ear, Nose, and Throat and Surgeon in charge of the Ear, Nose, and Throat Department, Royal Free Hospital. Aurist to the Queen.

K.B.E. (Civil Division)

CHARLES RITCHIE BURNS, O.B.E., M.D., F.R.C.P., of Wellington, New Zealand. For services to medicine.

FREDERICK HORACE SMIRK, M.D., F.R.C.P., F.R.A.C.P. Professor of Medicine in the University of Otago, New Zealand.

Knighthood

JOHN SMITH KNOX BOYD, O.B.E., M.D., LL.D., F.R.C.P., F.R.S. Brigadier, late R.A.M.C. (ret.). Director, Wellcome Laboratories of Tropical Medicine, 1946–55. President, Royal Society of Tropical Medicine and Hygiene. For services to bacteriology.

ALDINGTON GEORGE CURPHEY, C.B.E., *M.C.*, E.D., M.D., C.M., M.C.P.S. Honorary Colonel, the Jamaica Regiment. President, Legislative Council, Jamaica. For public services in Jamaica.

JOHN CAREW ECCLES, D.Phil., M.B., B.S., F.R.A.C.P., F.R.S., F.R.S.N.Z. Professor of Physiology, Australian National University, Canberra. For services to physiological research.

BENJAMIN THOMAS EDYE, C.B.E., F.R.C.S., F.R.A.C.S., of Sydney, New South Wales. For services to medicine.

KENNETH BARRON FRASER, C.B.E., E.D., M.S., F.R.A.C.S. Brigadier, late Australian Military Forces, of Brisbane, Queensland. For public services.

ERIC WILLIAM RICHES, *M.C.*, M.S., F.R.C.S. Surgeon and Urologist to the Middlesex Hospital. Consultant Urologist to the Army.

C.B. (Military Division)

LANCELOT MILLER CORBET, C.B.E., M.B., B.S. Acting Air Vice-Marshal, R.A.F. (ret.). Deputy Director-General of R.A.F. Medical Services.

JOHN HUSTON, M.B., B.Ch., F.R.C.S.Ed. Major-General, late R.A.M.C. Consulting Surgeon to the Army and Director of Surgery at the War Office. Honorary Surgeon to the Queen.

RICHARD LOUIS GIBBON PROCTOR, M.D., F.R.C.P.I., D.P.H. Surgeon Rear-Admiral. Deputy Medical Director-General of the Navy. Honorary Physician to the Queen.

C.B. (Civil Division)

GEORGE EDWARD GODBER, D.M., F.R.C.P., D.P.H. Deputy Chief Medical Officer, Ministry of Health.

C.M.G.

JAMES MALCOLM LISTON, M.B., Ch.B., D.P.H., D.T.M.&H. Director of Medical Services, Tanganyika.

RICHARD MURCHISON MORRIS, O.B.E., M.D., D.P.H., D.T.M.&H. Federal Secretary for Health, Rhodesia and Nyasaland.

C.V.O.

JAMES CROOKS, M.B., Ch.B., F.R.C.S. Ear, Nose, and Throat Surgeon to the Hospital for Sick Children, Great Ormond Street, London.

C.B.E. (Military Division)

ROBERT ARTHUR SMART, M.B., Ch.B., D.P.H. Colonel (temporary), R.A.M.C. Deputy Director of Army Hygiene.

DENIS AYMARD WILSON, A.F.C., F.F.R., M.R.C.S., L.R.C.P., D.M.R.E., D.M.R. Air Commodore, R.A.F. Honorary Surgeon to the Queen.

C.B.E. (Civil Division)

DANIEL FOWLER CAPPELL, M.D., F.R.F.P.S., F.R.S.Ed. Professor of Pathology in the University of Glasgow.

CHARLES SKINNER HALLPIKE, M.B., B.S., F.R.C.P., F.R.C.S., F.R.S. Aural Physician, National Hospital for Nervous Diseases and Director of the Otological Research Unit of the Medical Research Council.

JEAN MACIVER MACKINTOSH, M.D., D.P.H., D.P.A. Administrative Medical Officer of Health for Maternity and Child Welfare, Birmingham.

O.B.E. (Military Division)

WARREN JOHN BOYD, E.D., M.B., Ch.B. Lieutenant-Colonel, R.N.Z.A.M.C., Territorial Force.

DENIS HENRY DRYBURGH BURBRIDGE, M.R.C.S., L.R.C.P., D.P.H. Lieutenant-Colonel (temporary), R.A.M.C.

ROY BRASMERE DAVIS, M.B., B.S., D.P.M. Group Captain, R.A.A.F. Deputy Director-General of Medical Services, R.A.A.F.

FREDERICK LATHAM, M.D. Wing Commander, R.A.F.

O.B.E. (Civil Division)

BASIL GEORGE BROOKE, M.D. Chairman, Medical Board, Manchester, under the National Service Acts.

ALEXANDER MACKAY CALDER, M.B., Ch.B., F.R.C.S.Ed. Surgeon, Newtownards Hospital, County Down.

HERMAN ROBERT FREDERICK, M.B., Ch.B. General practitioner, Port Talbot.

ERNEST WIGHTMAN GINNER, M.D. Physician to Sunny Bank Hospital, Cannes.

ROBERT MERRICK LLOYD STILL, M.R.C.S., L.R.C.P. Medical Superintendent, Mental Hospital, Barbados.

STANLEY AUGUSTINE MCDONNELL, M.S. For services to the community in the Balonne area, Queensland, Australia.

ALASDAIR MCKELVIE, M.B., Ch.B., D.T.M.&H. Lately Specialist Leprologist, Ministry of Health.

LILY MARGARET O'HANLON, M.R.C.S., L.R.C.P. Head of Pokhara Mission Hospital, Nepal.

CECILY MARY WISE PICKERILL, M.B., Ch.B., of Wellington, New Zealand. For services in the field of plastic surgery.

ERIC BLAKE WILD, M.B., B.S., F.R.C.S.Ed. Doctor in charge of Church Missionary Hospital, Isfahan, Persia.

M.B.E. (Military Division)

CHARLES JOHN WILLIAMSON SOUTAR, M.B., B.S. Squadron Leader, R.A.F.

M.B.E. (Civil Division)

JACOB BENONI DAVIES. Chief Surgical Assistant, Sierra Leone.

CHARLES DONALD FERGUSON, M.B., Ch.B. For political and public services in Ross and Cromarty.

ARTHUR STEPHEN GARRETT, M.B., B.S. Medical Officer, Leprosy Service, Eastern Region, Nigeria.

GAVIN MUIR, M.B., Ch.B. Member, Medical Board, Newcastle upon Tyne, under the National Service Acts.

B.E.M.

BERTRAM THOMAS JOHNSON GLOVER, M.D., D.P.H. Chief Officer, Headquarters Section, Civil Defence Corps, Eastbourne.

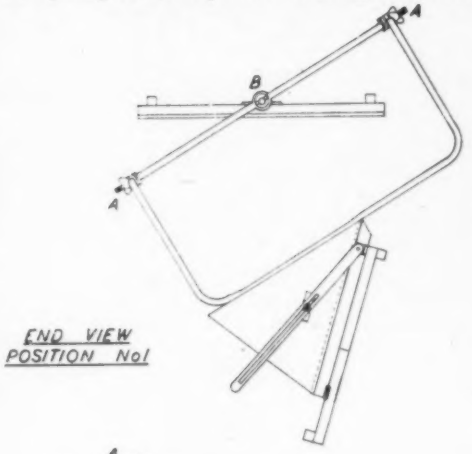
New Appliances

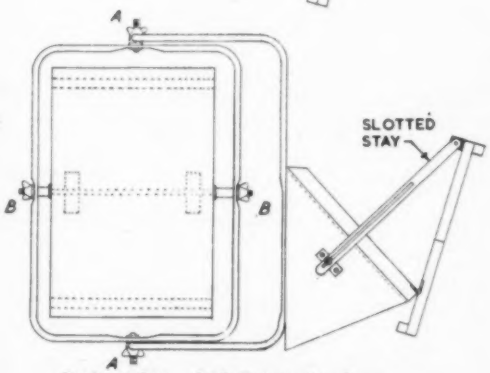
MIRROR-READING DEVICE TO FIT ON A RESPIRATOR

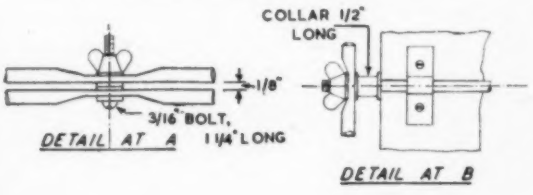
In the *British Medical Journal* of November 23, 1957 (p. 1237), Messrs. Theodore Hamblin described a mirror-reading device mounted on a Drinker respirator. The model illustrated below is claimed to have greater scope and to be almost as simple to construct. It has been thought out by Mr. I. M. Lambert, himself paralysed from the shoulder-girdle downwards, with little movement of the head, and has been in daily use by him and another patient at the City Infectious Diseases Hospital, Edinburgh, for about ten years. In addition to its usefulness for reading, television-viewing has been made easy for them.

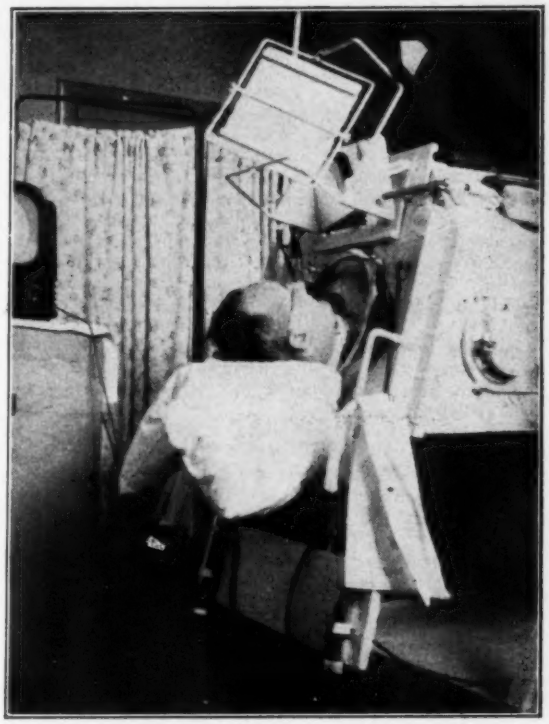
The wood and metal work can be undertaken by a joiner and a blacksmith (see Diagram), and aluminized surface-reflecting mirrors are strongly advised in spite of their high relative cost. These have shown no significant deterioration, so they can hardly be said to be very easily damaged.

The accompanying photograph shows the patient viewing television, with undistorted pictures, although for convenience the set is placed to one side, thus not interfering with the opening of the respirator. Reading can be done with the respirator open, and, with the mirrors set at almost the same angle, the patient can read a book placed on top of the respirator when this is closed. He always looks into the mirror closest to the end of the respirator, and in it sees the reflection from the larger mirror independently.









When playing chess, both patient and opponent face the same way, so this cancels out the mirror-image effect in describing the directions of the patient's moves.

Further details of the apparatus can be obtained from Mr. I. M. Lambert, at 14a, Dublin Street, Edinburgh, 3.

Motoring News

BRAKE LININGS

With the increase in performance of cars in recent years has come the need for improved braking systems and brake linings. This has resulted in considerable research on new braking materials in the larger manufacturing firms as greater stopping power is demanded on heavier and faster cars.

There are two main groups of linings—textile and moulded. Textile types consist of asbestos fibres woven into cloth, and the moulded types are asbestos fibres and other heat-resisting materials bonded together. Each has its own range of characteristics and properties. The disk brake, a British invention and one which is proving most successful on high-performance production sports cars and racing cars, and which will ultimately be fitted to the popular range, is the latest development in braking systems. Its chief advantages are that it is not susceptible to fade, it is light, and the small friction pads, which can be cheaply manufactured from hard-wearing, heat-resisting bonded materials, can be very quickly replaced.

Many motorists sometimes do not realize quite how many different types of linings are available for their cars. For the average car a compromise between no fade in conjunction with high pedal pressure and slight fade with light pedal

pressure must be reached. In general the former is better suited to the sports car or rally driver who wants to be able to lock all four wheels at speed and the latter to the more sedate driver with a large heavy car.

The Cape Asbestos Company market their "Capasco" HF32, which comes into the first category for use on faster cars; it has a high coefficient of friction, with exceptional resistance to fade. "Capasco" HF33 is smoother and wears better, being more suited to the normal car; "Capasco" BR20 is ideal where medium friction linings are needed and where servo assistance is available. Ferodo MR19 is a solid woven non-metallic material suitable for medium-sized cars; DM7, moulded, is better for light to medium models and has a high friction value, while DM8, also moulded, has alloy chippings for better heat dispersal and is designed for high-performance cars. Small and Parkes Ltd. offer Don R14, an entirely satisfactory lining for normal use, giving a smooth and progressive action at the brake pedal. Don 24, 424, and ML2 are pressure-moulded examples for fast heavy cars; they do not fade readily at high temperatures, but are not so long-lasting as Don R14.

So if the time has come for new brake linings to be fitted to your car a word or two with the garage man beforehand can mean quite a difference to the pleasure of driving and the handling of the car.

Touring Topics

A series of nine leaflets dealing with the main holiday regions of Spain and the hotels and pensions therein is now available from the Spanish National Tourist Office, 70, Jermyn Street, London S.W.1. Each leaflet deals with a specific area, gives information on the customs, foods, and festivals of each, while supplementary leaflets give details of the small villages and quote the hotels and pensions and give their addresses. These are well worth while obtaining if Spain is your objective for holidays this year.

The Michelin Guide *Camping en France* is a great asset to those who wish to live under canvas in France. Supplies are now limited owing to the immense demand, but copies are available at leading booksellers.

Motorists seeking a less strenuous holiday in France may be interested in a new publication by the French Government Tourist Office, 178, Piccadilly, London, W.1. This is the most recent of a series of 80-page booklets entitled *Itineraries in France* and deals with the region east of Paris—one which many visitors pass through on their way to Switzerland but also one which has many hidden charms. With strip maps and pencil drawings, features at which the French are most adept when it comes to travel guides, the areas of the Vosges, the Champagne country, Strasbourg, and the vineyards of Alsace are comprehensively described, together with notes on the special foods and wines of the region. Like its predecessors on the North of France, Normandy, Paris—Côte d'Azur, it is issued free in an English edition.

On June 28–29 Aix-les-Bains is holding a Lake Festival which will include a 24-hour race for speedboats and a race for children's petrol-driven cars.

The Larger Vauxhalls

The Vauxhall has always been a popular car in Britain in spite of its close associations with General Motors Ltd., of America.

The small 1½-litre Victor has been on the market here for some time, but the latest type Velox and Cresta models are comparatively new. A brief spell at the wheel of the de-luxe Cresta recently made me realize that, although this is a large car as overall dimensions go, it is light to drive and easy to manœuvre. Visibility is exceptionally good, and the view from behind the wheel almost perfect.

At first sight these cars would appear to be too big for everyday town use and certainly inconvenient for the average general practitioner, but with their feather-light

(*Continued at foot of next column*)

(*Continued from preceding column*)

steering, good visibility, and a turning circle of 34½ ft. (11 m.) they are easily manageable in confined spaces. Comfortable accommodation for five or even six passengers and luggage space to match are desirable features. Petrol consumption varies on either side of 24 m.p.g., depending on how the car is driven.

Prices always seem to be on the up and up, and the Velox will now relieve you of £983 and the Cresta of £1,073 with the tax paid. Both these figures represent quite large slices of anyone's spending money, but Vauxhalls have always given value-for-money motoring, and these two larger models are simply offering more comfort and more luxury for a little more money.

IAIN GELLATLY.

To-day's Drugs

In this column we publish from time to time authoritative notes on a selection of drugs in current use.

Plaquenil (Bayer Products Ltd.).—Tablets of this substance contain 400 mg. of hydroxychloroquine sulphate. Its use is advocated in the treatment of discoid lupus erythematosus and other "light sensitive" diseases, in the treatment of rheumatoid arthritis, and in the treatment and suppression of malaria. It may also be given for giardiasis, 600 mg. daily in divided doses for five days. For the first two conditions the suggested dose is 400 mg. once or twice daily. A three-day course totalling 2 g. is advised in the treatment of malaria, one tablet of 400 mg. weekly in its suppression.

Toxic effects are said to be fewer than with chloroquine and better tolerated, but headache, gastro-intestinal disturbance, pruritus, and lassitude may occur. This claim to a lower incidence of toxic reactions is the main reason for the drug's introduction, for the administration of chloroquine in the treatment of rheumatoid arthritis has caused several unpleasant side-effects except when it is given in small dosage. In the treatment of this disease immediate improvement is not to be expected; two to four weeks or more of continuous therapy is said to be necessary before any improvement is seen. In the opinion of most workers the efficacy of hydroxychloroquine sulphate and its proper place in the treatment of rheumatoid arthritis still remain to be defined. Because the drug is known to concentrate in the liver, it should not be given to patients with hepatic disease.

N.H.S. basic price: 100 tabs., 90s.

Distaval Tablets and **Distaval Forte Tablets** (Distillers Co. (Biochemicals) Ltd.).—These tablets contain thalidomide, or N-phthalyl glutamic acid imide. There is 25 mg. in each distaval tablet and 100 mg. in each distaval forte tablet.

This substance was introduced in 1955 in Germany, where it has been widely used as a daytime sedative (25–50 mg. two to four times daily) and to induce sleep at night (50–100 mg.). Its hypnotic action lasts for 4–6 hours, so that its effect resembles that of the medium-acting barbiturates such as butobarbitone. The early clinical reports indicated that it was virtually free from harmful side-effects, and no toxic symptoms could be produced in animals by the highest doses which solubility permitted. Recently, however, it has been shown to have a mild but definite antithyroid effect when given in doses of 200 mg. or more. It suppressed the uptake of radioactive iodine in normal subjects and lowered the basal metabolic rate in hyperthyroid patients. At present the mechanism of this antithyroid action is unknown, and prolonged administration of thalidomide is not advisable until more is known about it.

N.H.S. basic price: distaval, 100 tabs., 10s. 10d.; distaval forte, 100 tabs., 29s. 0½d.

Correspondence

Casualty Clearing

SIR,—This subject is one of great and pressing national interest. It is perhaps unfortunate that the emphasis now seems usually to fall on the organization for "the major accident." This is due no doubt to the fact that the major accident is front-page news, while the enormous daily toll of casualties is taken for granted. Paper plans for dealing with major accidents will be of value in direct proportion to the efficiency of the accident service organization which operates continuously in the area in which the accident occurs. The outside problems of the major accident such as transmission of information, breakdown of telephone services, transportation of injured—of these we had first-hand experience in the Didcot rail crash of November, 1955—can all be dealt with effectively by prepared mobilization of police and ambulance services. The essential feature in dealing efficiently with the casualties is the existence of an organization in all key hospitals accustomed to dealing each day with large numbers of casualties and capable of immediate expansion to meet any sudden need.

The last sentence of the annotation (*Journal*, June 7, p. 1345), "but, as finance allows, should not more provision be made for treating the million or more people who receive hospital treatment for accidental injuries every year?" should surely be emphasized as a positive need now, rather than a questioned need of some future date.—I am, etc.,

Oxford. J. C. SCOTT.

SIR,—In your review of the report by the senior administrative medical officer of the South-east Metropolitan Regional Hospital Board on the Lewisham train disaster (*Journal*, June 7, p. 1345), I was rather concerned to learn the report stated that the mobile medical teams "were unanimous that all that was needed was supplies of morphine and simple shell dressings."

While no one would deny that morphine has a place in the treatment of severe pain, it has been my experience that it is frequently administered to patients suffering from shock where pain is only of slight or moderate degree. One of the few things which are known about shock is that it is associated with a reduction in the volume of circulating blood either by direct loss to the exterior or by pooling in the vessels of the abdominal viscera. The shocked patient is already suffering from anoxia, and the administration of morphine may result in a sufficient depression of respiration to lower the cerebral oxygen supply beyond the minimal requirements and thereby kill the patient. The treatment of shock is adequate transfusion, preferably with whole blood, but, if this is not available, with plasma or dextran. This has been repeatedly emphasized in your own and other medical journals. Pain accompanying severe injuries can usually be relieved by other and safer drugs such as pethidine.—I am, etc.,

Pennington, Hants. MICHAEL B. CARSON.

Induction of Labour

SIR,—In their article "Surgical Induction for Suspected Placental Insufficiency" (*Journal*, May 24, p. 1211), Mr. Ian Cope and Mr. Morton G. Pearson state that although the incidence of surgical induction of labour in the Hammersmith Hospital increased seven-fold between 1951 and 1956, with an unchanged overall caesarean section rate, the overall perinatal mortality rate did not fall. It is inferred that induction of labour for placental insufficiency has little or no value and may be risky. I feel that it would be a pity to let these findings pass without comment, because in the Aberdeen Maternity Hospital a policy of routine induction of labour in selected cases, together with the greater use of caesarean section for foetal distress as the main indication, has been accompanied by a fall in perinatal mortality at a time when national rates, like those in the Hammersmith Hospital, have remained static. (Between the years 1948–52 and 1953–7 the perinatal mortality in Aberdeen fell from 32 to 26 in all parities and from 37 to 27 in primigravidae.) I am anxious that this policy, which has been successful here, should receive an adequate trial elsewhere.

The policy, which is described below, is not negatived by the results of Cope and Pearson. Their incidence of induction of labour rose only to 14.6% in 1956; the average in Aberdeen during the past five years has been 23.6%. The table giving indications for induction of labour in Hammersmith shows that of 185 additional inductions performed in 1956 as compared with 1953, only 16 were for postmaturity; in Aberdeen, the majority of inductions performed *routinely* are in pregnancies not ending spontaneously before the end of the 41st week of pregnancy. In some of those cases mild hypertension is present, but in our experience this does not increase the risk of foetal death and we do not consider mild hypertension by itself as an indication for induction. In Hammersmith, the increase of induction has not been accompanied by a rise in the overall incidence of caesarean section; this is difficult to understand, since it is claimed that caesarean section has been undertaken more frequently after induction. The Hammersmith results are reported for all parities and all age-groups; in Aberdeen, special attention is paid to the elderly primigravida, in whom the dangers of placental insufficiency are greatest. Finally, it may be of importance that admissions to Hammersmith Hospital are highly selected; if this is not so, the rates of caesarean section (over 5%) and of perinatal death (about 37 per 1,000) are surprisingly high.

The Aberdeen policy is based on a number of epidemiological and clinical facts, which may be summarized as follows. "Unexplained" death of a mature foetus—presumably the result of an inadequate placental reserve—is favoured by three general factors: primiparity, high maternal age, and prolongation of pregnancy past term. Foetal death may occur unexpectedly before the onset of labour, so that it is difficult to anticipate, or so suddenly during the course of normal labour that there is no time to rescue the baby.

Using these facts, we decided in 1953 to puncture the membranes in all primigravidae aged 25 years or over in whom labour had not started before the end of the 41st week. If the liquor amnii was stained with meconium, caesarean section, elective or after a short trial of labour, was to be considered, in the interests of foetal survival; decisions to undertake section may, of course, be weighted by other factors, such as maternal age and parity, the presence or absence of hypertension, the length of time the membranes have been ruptured, and the course of labour. This policy seemed to be so successful initially that it rapidly spread to younger primigravidae and to multigravidae.

The Table below shows the results in 1953–7 compared with 1948–52, in primigravidae by age, and in multigravidae. Per 1,000 maternities, about 6 perinatal deaths have been prevented at a cost of 145 more surgical inductions and 14 more caesarean sections. The gains are much higher than average in primigravidae aged 30 years and over, but younger primigravidae and multigravidae are so much more numerous that the lesser gains in these groups assume considerable importance in the overall figures. It should be noted that the striking rise of perinatal

Aberdeen Maternity Hospital: Booked Legitimate Maternities (City Residents)

Primigravidae	No. of Cases		Surgical Induction Rate (%)		Caesarean Section Rate (%)		Perinatal Death Rate (per 1,000)	
	(a)	(b)	(a)	(b)	(a)	(b)	(a)	(b)
15–24	2,800	3,093	8·4	23·7	1·0	2·3	34·3	28·5
25–29	1,096	1,286	8·9	28·0	2·7	5·8	32·9	26·4
30–34	323	353	12·1	34·8	6·8	11·6	49·6	19·8
35+	145	100	15·2	39·0	24·8	32·0	89·7	20·0
Primigravidae all ages ..	4,364	4,832	9·0	26·0	2·7	4·5	36·9	27·1
Multigravidae	6,687	7,465	9·2	22·0	2·3	3·3	28·7	25·3
All parities ..	11,051	12,297	9·1	23·6	2·4	3·8	32·0	26·2

(a) 1948–52. (b) 1953–7.

mortality with age in primigravidae during 1948–52 has been eliminated in 1953–7; in Aberdeen the "elderly primigravida" now has a lower risk of losing her baby than most mothers. The persistence of a rising trend of mortality with age in national statistics forms a contrast and constitutes a challenge.

Obstetrical management in general has improved in Aberdeen during the years under examination—as it has no doubt done elsewhere—and the policy outlined above is not solely responsible for the reduction of perinatal mortality. But these results, which have been much more thoroughly examined than can be shown here, are most unlikely to be due to chance, and it therefore seems justifiable to draw attention to them together with the policy which I believe to have been partly responsible.

In your leading article on Cope and Pearson's paper, you note that there is at present no adequate method of assessing placental function, and that "the obstetrician still has to rely on his clinical judgment in deciding afresh in each case whether induction of labour will be of benefit to the baby's health or not." If the obstetrician relies entirely on his judgment of the individual case, he will lose the occasional baby because of the absence of reliable indications of "placental insufficiency." The alternative is to perform numerous routine inductions of labour on the basis of epidemiological inference and to use caesarean section freely in the interests of the baby, in order that at least some of these sudden deaths from asphyxia may be prevented. The disadvantages of our policy are the large numbers of inductions which have to be performed to save the lives of relatively few infants, and the risk of introducing infection. On balance we think that it has been justified in the absence of any more selective method of prevention.—I am, etc.,

Aberdeen DUGALD BAIRD.

SIR,—The observations and conclusions of Mr. I. Cope and Mr. M. G. Pearson (*Journal*, May 24, p. 1211) and your leading article (p. 1226) on the induction of labour draw attention to the cult of interference which has become the priority danger of childbirth. Interference has been made increasingly safe in the last hundred years by the use of antiseptics, antibiotics, and anaesthetics. There is a sense of security in action which is more acceptable than patience when in conflict with uncertainty. Early interference in obstetrics, without clinical indication, is prompted by ignorance, fear, or convenience. Inadequate clinical experience and responsibility beget doubts and anxieties.

The comparison of the changing statistical pictures of 10 to 15 years ago and to-day in reference to induction and other forms of interference in childbirth is interesting. Chester Bradley,[1] reporting on a series of 1,041 cases, writes: "Inductions . . . 10, i.e. 0.96%. Caesarean Sections 1.2%. Seven years ago, Hammersmith rate of induction was 2.1%, two years ago it was 14.6%."

In the United States of America this year I learned of "induction by appointment." In some hospitals from 50–70% of all pregnancies are terminated by induction. A senior gynaecologist in Seattle told me that he induced over 70% of his cases. At other hospitals in different States this interference was accompanied by forceps deliveries (between 45 and 80%) and episiotomies (100%) as a routine; breast-feeding was not encouraged, isolation of the husband from the birth incident was the rule. Drugs and anaesthetics were exhibited throughout or during all labours. This cult of interference with normal childbirth has undoubtedly grown in good faith and has been prompted by humane and kindly motives. It is more highly developed in the U.S.A. than in any other country in the world—I was assured it was the only way to conduct midwifery. No evidence can be supplied, however, to support this contention but the significance of a report by Nicholson Eastman[2] is in its association with childbirth. He writes: "Some half million of our (U.S.A.) children and youth are afflicted with cerebral palsy, with ten thousand new cases at birth every year. Approximately 300,000 suffer from epilepsy and no less than one and a half millions are mentally retarded." He attributes two-thirds of all cases of cerebral palsy to obstetric factors. Other observers put it higher.

I cannot describe, in a short communication, the impact of interference with healthy childbirth upon the minds of women, except to emphasize its noxious effects. The observation, Sir, at the end of your leading article, "The obstetrician has still to rely on his clinical judgment," will, we hope, make a deep impression on all who practise and teach normal as well as abnormal obstetrics. In this we may be well advised to go forward with the other great school of American obstetricians, which is rapidly replacing modern sensate mechanisticism by an ideational and purposeful approach. In this, the physiological and the natural is accepted as the perfect creative function and the boon of science employed only to protect the healthy from assault and to rectify the reproductive faults, environmental and cultural, that do, and always will, occur. The clinical and educational procedures designed to attain that end minimize the need for interference. Induction, caesarean section, episiotomy, and anaesthetics are immediately employed when indicated by signs and symptoms. Hospitals dedicated to this teaching are scattered throughout the States, and from experience it has been learned that interference is rarely necessary in healthy women. The mind will frequently exclude the cause of trouble and therefore its results.

Familiarity with the natural and physiological law has enabled us to explain, and so avoid, the cause of many defects in cultural reproduction. Observations on women already made pathological by interference may demonstrate the details of disturbance but will only complicate the search for causes.—I am, etc.,

Chichester. GRANTLY DICK-READ.

REFERENCES

[1] Bradley, C. D., *N.C. med. J.*, 1949, **10**, 343.
[2] Eastman, N., *Pediat. Clin. N. Amer.*, 1957, **4**, 1995.

Dummy Tablets

SIR,—Articles often appear in the journals describing carefully controlled investigations into the use of therapeutic substances of unproved value in minor ailments. Generally tablets are handed out to groups of patients and their subjective and objective reactions analysed. The basis of the experiment is the contrasting of a drug-containing tablet against a dummy tablet containing an inert substance. This is easy enough to arrange in hospital or clinic where the patients have their prescriptions dispensed at the pharmacy on the premises and special arrangements can be made to have the inert tablets ready, but it cannot be managed in the majority of non-dispensing practices.

I am sure there are many practitioners, like myself, who would be glad to conduct some investigation into the relative values of the mass of proprietary drugs now being foisted upon us. Many are obviously made only to sell and it is impossible to judge their usefulness, if any, without some control substance to use in a parallel series of cases or to substitute during the course of treatment for the proprietary article. If the *British National Formulary* contained some control tablets of inert substances a great deal of difficulty of investigation in general practice would be overcome. I suggest that *Tab. Normalis Rubra* or *Tab. Whitehall Co.* should be introduced and perhaps made available in a choice of colours. Even if there are not a sufficient number of scientifically minded practitioners to make the inclusion of these tablets worth while for experimental work, there is a very good case for the inclusion of a genuine placebo which will cost next to nothing to the National Health Service. I am pretty sure I could make good use of such an item in my practice, to the benefit of my patients, my soul and conscience, and the Chancellor of the Exchequer.

We are being exhorted to cut down on prescribing and to give our patients health talks instead of boxes of tablets. But we receive very little positive help from the Ministry of Health to further this laudable advice. Like Mr. Punch's patient who has "'ad 'er diet" and is now going to have her dinner, the patients listen tolerantly to our health talks but still want a remedy as well. Short of complete reorganization of the patients' social background and immediate liquidation of all their financial commitments under the hire-purchase system, what better than *Tab. Normalis Nigra* for that dizziness and *Tab. Whitehall Co.* for lack of energy ?—I am, etc.,

Sheffield, 8. E. C. ATKINSON.

Malignant Exophthalmos

SIR,—I wish to record the fact that a few weeks ago I secured a dramatic cure of a case of malignant exophthalmos (ophthalmoplegic exophthalmos) by the use of acetazolamide. This drug has not previously been used or suggested in the treatment of this condition so far as I can ascertain from a search of the literature.

Dosage was the same as is used in the treatment of glaucoma, i.e., one 250 mg. tablet twice daily, reducing to once daily, and was combined with potassium bicarbonate, 1 g., thrice daily. The exophthalmos was gross, had resisted every form of treatment for over twelve weeks, and was on the point of being dealt with surgically by orbital decompression. The proptosis responded with extraordinary rapidity in under 48 hours, and became minimal after a further few days. Muscle movements returned, but the fibrotic changes in the superior rectus and levator palpebrae muscles were not prevented in time, so that upward movement of the eyeball and retraction of the upper lids have only partially recovered. Thyrotoxicosis was not prominent at the stage the acetazolamide was tried, but in spite of this the effect on the patient's general condition was excellent.

Severe cases of malignant exophthalmos are fortunately infrequent, and makes it difficult for the individual practitioner to base his communication on a series of similarly treated patients. It is hoped that this letter will make it possible for other cases to be considered for treatment at once, and preferably in a much earlier stage of the disorder before irreversible secondary changes have developed in the ocular muscles and orbital fat. The drug is also to be tried out now empirically in less severe cases of toxic goitre in an endeavour to discover if it can exert similar curative therapeutic effects.

A paper giving further details of this case has been prepared for publication.

—I am, etc.,

London, W.1. LIONEL M. GREEN.

Suppuration in Rheumatoid Arthritis

SIR,—With reference to the paper by Professor J. H. Kellgren and Drs. J. Ball and R. W. Fairbrother and Mr. K. L. Barnes (*Journal*, May 24, p. 1193), we have recently had a case at this hospital which may prove interesting.

He was 78 and had been diagnosed at the Middlesex Hospital as having rheumatoid arthritis in 1955, and was put on prednisone 5 mg. thrice daily. He was seen here in October, 1957, when his knees were not particularly affected. As his condition improved the dose was reduced to 2.5 mg. twice daily. On February 26, 1958, he was seen again, when he complained of acutely painful joints, mainly the knees. His doctor had increased the prednisone to 10 mg. thrice daily.

On examination he was ill, with numerous swollen joints; the left wrist was so painful that it was supported in plaster. His right knee was so swollen that it was aspirated and purulent fluid found containing coagulase-positive *Staph. aureus*, sensitive to nearly all the wide-spectrum antibiotics. He was admitted to hospital and given soluble penicillin, 1,000,000 units six-hourly. He was in hospital four days, and developed a painful swelling over the left temporo-mandibular joint. His condition deteriorated rapidly, and he died on March 2.

Post-mortem examination showed thick pus in all the joints opened, including both knees, right wrist, and both sternoclavicular joints. He also had bronchopneumonia.

Death was presumed to be due to bronchopneumonia from staphylococcal suppurative polyarthritis.

I am indebted to Dr. J. W. Todd for allowing me to write up this case.

—I am, etc.,

Farnham, Surrey. T. G. L. ALLUM.

SIR,—We were very interested to read the article by Professor J. H. Kellgren and his colleagues in the *Journal* of May 24 (p. 1193) on suppurative arthritis complicating rheumatoid arthritis. A similar case has recently been admitted to the Brook General Hospital under the care of Dr. G. E. Loxton.

This patient is 69 years of age and his occupation was formerly that of a pile driver. He has suffered from rheumatoid arthritis for eight years, all the limb joints having been affected. An arthrodesis of the left knee had been performed four years earlier. Eighteen months before admission sinuses developed at both elbows which had discharged small quantities of pus for two to three days every month. Two weeks before, he experienced general malaise and fatigue and the sinuses began to discharge again.

On examination he was ill, looked anaemic, but was afebrile and there was no lymphadenopathy. Gross rheumatoid changes were found in all the limb joints. Rheumatoid nodules were present on the ulnar border of the forearms and on the shins. There were sinuses discharging large quantities of pus at both elbows, also a healed sinus, which later broke down, under the metatarso-phalangeal joint of the right big toe. *X*-rays of the joints showed advanced rheumatoid change with complete disorganization of the wrist joints and subluxation of the metacarpophalangeal joints. Chest *x*-ray showed old tubercular scarring at the apices. A barium meal was also performed as there was a 20-year history of vague epigastric pain of short duration unrelated to meals. This revealed a small sliding para-oesophageal hernia and appearances suggestive of ulceration of the duodenum. Hb 35% (5.1 g. per 100 ml.); W.B.C. 7,000; E.S.R. 78 mm./1 hour. Examination of the bone marrow showed an iron-deficiency anaemia with evidence of active haemopoiesis and chronic sepsis as shown by 9% plasma cells. Urinary urobilinogen, serum bilirubin, and cell fragility tests were normal. Cold agglutinins were found in the blood. W.R. was negative. Of three stool specimens tested for occult blood one was positive: the severe degree of anaemia would therefore appear to be partly due to blood loss through the gastro-intestinal tract. Serum proteins: total 5.8 g., albumin 2.9 g., globulin 2.9 g.; electrophoretic pattern showed a marked reduction of albumin. Of three blood cultures taken, two have been negative so far, but one has shown a pure growth of *Staph. pyogenes*. Pus from the sinuses showed *Staph. pyogenes* on culture. No acid-fast bacilli were seen in stained films—cultures are in preparation.

The following treatment was given: 3 pints (1.7 l.) of blood were transfused and a course of an iron-dextran complex was started, while splinting and soluble aspirin were used to relieve joint pain. The staphylococcus grown was relatively insensitive to antibiotics other than chloramphenicol and novobiocin, and treatment was started with the latter. The patient's progress so far has been good; his general condition has improved, he has remained afebrile, and his E.S.R. has fallen from 78 mm. to 57 mm.

We would like to thank Dr. Loxton for encouraging us to report this case and the *x*-ray and pathology departments for their kind assistance.

—We are, etc., PAUL ATKINS.
J. J. BRAND.

London, S.E.18.

Polio Vaccination

SIR,—Like your correspondent Dr. G. H. Pimblett (*Journal*, May 31, p. 1299) we have had a few puzzling reactions to poliomyelitis vaccine—both British and Salk types of vaccine. They have occurred in six children, aged 1 year to 6 years, following the first inoculation; none have been reported after the second inoculation. The reactions have been characterized by an unwillingness to walk. The onset varied from 24 hours to 1 week after the inoculation and the duration from 12 hours to 48 hours. Recovery was always complete. In one case, a colleague's child, a temperature of 103° F. (39.4° C.) was recorded and vertigo was a symptom. A mother who has had experience of poliomyelitis in her family described the reaction as similar to the onset of poliomyelitis in her other child. In two cases, faecal samples were examined by Professor G. W. A. Dick and Dr. D. Dane, Queen's University, Belfast, for the presence of live virus, with negative results. Similar samples from the parents in one of these cases were also negative.

We have not seen these children in the acute stage and offer no explanation of the reactions—the absence of live virus is reassuring. The six cases occurred among 17,000 children receiving two injections each. This compares with four typical allergic skin eruptions among the same total.—We are, etc.,

N. DONALDSON,
W. J. MCLEOD.

Belfast.

SIR,—Further to the letter from Dr. Joan Newton (*Journal*, May 31, p. 1299) it is noteworthy that the observations of many investigators have shown that tonsillectomy

seriously increases the risk of contracting the dangerous bulbar forms of poliomyelitis. It is important to appreciate that this risk, although greatest during the first month after tonsillectomy, remains elevated for many years thereafter. Anderson and Rondeau[1] estimated that, during the 1945 epidemic in Minnesota, previous tonsillectomy increased fourfold the risk of contracting bulbar poliomyelitis. During the 1952 epidemic in the same area, Paffenbarger[2] calculated that attack-rates in tonsillectomized and non-tonsillectomized groups were in the ratios of 1.7:1 for all forms of poliomyelitis, 6.4:1 for bulbospinal, and 9.6:1 for pure bulbar forms of poliomyelitis. These differences were not explicable in terms of age, sex, socio-economic status, stage of epidemic, history of tonsillitis or colds, or reasons for tonsillectomy. The Medical Research Council's[3] investigation during 1951–3 confirmed that in Britain also "persons whose tonsils had been removed were more likely to develop the bulbar forms of poliomyelitis than those who had not had the operation, even if years had elapsed between the removal of the tonsils and the onset of poliomyelitis."

These facts merit consideration by the doctor faced with the decision whether his patient's tonsils should be removed. If tonsillectomy is deemed essential, it would seem proper to complete an immunizing course of poliomyelitis vaccine beforehand.—I am, etc.,

Glasgow, N.W. N. R. GRIST.

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[2] Paffenbarger, R. S., *Amer. J. Hyg.*, 1957, 66, 131.
[3] Medical Research Council, *Lancet*, 1955, 2, 5.

SIR,—I agree with Dr. D. E. Parry Pritchard's letter about polio vaccination (*Journal*, May 24, p. 1235). With a team consisting of a medical officer, a health visitor, and a clerk there is little difficulty in carrying out 200 polio vaccinations in a two-hour session. Planning and the application of a little time-and-motion study make it possible to cut out delays and to speed up some of the processes; for instance, the use of very wide-bore needles for drawing up vaccine into the syringe saves many seconds, and small 1-ml. syringes are light and easy to handle quickly.

In dealing with large numbers it is more than ever necessary to make sure that the sterilization technique is faultless, and not rushed in any way. Appointments are staggered and we try to ensure that people are not kept waiting about unnecessarily, a point that is greatly appreciated. Children of all ages attend the sessions; and I think that this is an advantage, for, if there is some slight delay in getting a toddler into position, the time can be used to change a batch of needles or open a fresh bottle of vaccine. Speeding up the technical details of injection does not imply that the children undergoing vaccination must be made to feel that they are coming through on a conveyer-belt. In 200-a-time sessions it is quite possible to treat each person as an individual, and this is what we try to do.

In conclusion, may I say what a poor and outdated instrument the hypodermic syringe is for giving large numbers of identical injections in a short space of time. Surely by 1958 we could have evolved a more efficient appliance, something with a pistol grip, a reservoir of vaccine, and a magazine of needles that could be rotated into position for each person. The present method is rather like rubbing two sticks together to light a fire.—I am, etc.,

Ipswich. KATHLEEN M. HARDING.

Monkeys for Polio Vaccine

SIR,—In your annotation (*Journal*, May 17, p. 1168) headed "Monkeys for Poliomyelitis Vaccine" you deplore the fragility and cost of these thousands of animals. The resolutely blind eye you turn on every other consideration must have amused many of your readers, including those disposed to play the Walrus to your Carpenter. The Walrus was just a little sorry.—I am, etc.,

Manchester, 14. J. L. DOBBIE.

Out-patient Gynaecology

SIR,—I was pleased to see Mr. Aleck Bourne's letter (*Journal*, June 7, p. 1352) supporting the findings of Mr. Norman Morris and Dr. Desmond O'Neill (*Journal*, May 3, p. 1038), especially as it corrects the misleading views aired by another gynaecologist who stated that he "found it difficult to believe that emotional stress alone can actually *initiate* gross symptoms, particularly pain" (*Journal*, May 17, 1177).

There is an aspect of this subject not yet mentioned in the correspondence that I would like to raise. In the same way that there are certain postulates accepted when considering the causation of bacterial disease, so there are definite criteria applicable to those conditions that are somatic reactions to emotional stress: (1) The condition begins at a time of emotional stress or crisis; (2) its course varies with the degree of stress; and (3) it clears up, or improves, following psychotherapy, or alteration in the stressful situation. It is the third of these criteria that I wish to deal with here, since it can only be tested and fulfilled by allowing a lot more time than might usually be available for any one patient in a gynaecological out-patient clinic. In my practice, it is constantly being applied and found to be true for patients suffering from such gynaecological disorders as amenorrhoea, menorrhagia, premenstrual tension, dysmenorrhoea, frigidity, dyspareunia, and the difficult climacteric.

I think a fourth criterion might well be added—that there is little or no lasting improvement where the treatment has consisted of drugs, or other physical means, without taking into account the importance of the emotional state of the patient. Any doctor who considers his patient as a person, and not merely a vehicle for a disease process with symptoms, will know the importance of emotional factors in all illnesses, and particularly so in gynaecological disorders. He will also know that the majority of women who have been subjected to a therapeutic "D. & C." have not had any lasting benefit and certainly do not show any desire for a repeat performance.

Mr. Morris and Dr. O'Neill are to be congratulated on bringing to our notice the importance of emotional tension as a cause of those illnesses in women for which they are frequently referred to a gynaecology clinic, and it would seem now to be our task to provide treatment which should be directed at the patient herself rather than at the symptoms.

London, N.W.3. PHILIP HOPKINS.

Do Sebaceous Cysts Exist?

SIR,—Many specimens are submitted from the casualty department accompanied by a paper bearing the diagnosis "Seb. cyst." In some 30 years of endeavour I have failed to substantiate this diagnosis. Of course, many of the specimens are not cysts: primary and secondary neoplasms have often been regarded—possibly because central necrosis has rendered them soft—as "cysts." In my experience the specimens that prove to be true cysts are usually of the "epidermoid" variety, their wall being composed of stratified squamous epithelium but without appendages, and their contents of shed squames; thus they seem to show no evidence of origin from the sebaceous glands.

Lund[1] stated of "sebaceous cysts": "There is no agreement as to what is meant by this term. . . . In my own experience distinct unquestioned sebaceous cells are not present and a separate classification from epidermoid cysts on the criteria offered above is not justified." (The criteria mentioned were nature of contents, demonstration of sebaceous cells in wall of cyst and lack of keratinization.) Probably the appearance to the naked eye of decomposed shed squames has suggested the term "sebaceous." The derivation appears to be from the Latin *sebum*—fat,

tallow—and accordingly any object resembling tallow might be so called. However, this is not to say that the contents of the cysts were ever produced by sebaceous glands. Clearly, tallow is not so produced. In Ackerman's *Surgical Pathology*[2] is the statement, "True sebaceous cysts are lined by sebaceous cells. . . ." But I cannot recollect ever seeing such a specimen.

It is submitted, therefore, in all seriousness, that one of the commonest conditions diagnosed in the casualty department either does not exist or at best is exceedingly rare. It is further submitted that since surgeons still apparently teach that it occurs frequently—and is diagnosable—they should produce evidence. In default of such evidence I suggest a more critical evaluation of "Seb. cysts." "Epidermoid cyst" is perhaps the best current term for the cyst composed of stratified squamous epithelium, without appendages, and whose contents are shed squames.—I am, etc.,

Sheffield. J. L. EDWARDS.

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[2] Ackerman, L. V., *Surgical Pathology*, 1953, p. 95. Kimpton, London.

Topical Steroids for Skin Conditions

SIR,—I have recently carried out a small therapeutic trial of prednisolone ointment, the results of which seem worth publishing.

The trial was carried out on in-patients, and the effect of 0.25% prednisolone was compared with 1% hydrocortisone, each used in a water-miscible base. When local steroid hormone treatment was ordered by me, the test substances were dispensed to alternate patients by the sister in charge and I was ignorant of which application the individual patient was given. Thirty patients in all were treated, the ages varying from 12 to 80, and the diagnoses being Besnier's prurigo, intertrigo, flexural psoriasis, "varicose" dermatitis, solar dermatitis, contact dermatitis, exfoliative dermatitis, and endogenous eczema. On final analysis, at the conclusion of the test, the age, sex, and diagnoses were found to be almost identical in the two groups.

The results of all the applications were noted at the time as being "satisfactory," no difference being noted then or on analysing the notes subsequently. Prednisolone is approximately four times as active as hydrocortisone when given systemically, and it now appears that it is equally potent when used topically. In general, a greasy base is more efficacious than a water-miscible base as a vehicle for hydrocortisone, and the same will probably be found for prednisolone.—I am, etc.,

London, W.1. PETER BORRIE.

Ethanolamine Oleate

SIR,—For many years I have used ethanolamine oleate as the sclerosant in the treatment of varicose veins by injection, but recently I encountered an alarming reaction to it.

I was treating a woman of 32 with only moderate varicosities. When she came back for her second injection a week after the first she complained of having had a severe rigor in the night after the first. She had been shivering and shaking for about half an hour. Although this might have had nothing to do with the injection, I decided to give her a much smaller dose the second time to be on the safe side. But again she had this alarming rigor during the night. Obviously she was allergic to ethanolamine oleate.

Apparently this is not common, for Bailey and Love in their well-known textbook *A Short Practice of Surgery* (10th edition, 1956) write of the drug: "Allergy can occur, but only after a prolonged course which, with modern treatment, should not be necessary." In the present case the reaction occurred after the first injection, however.—I am, etc.,

Merioneth. CLAUD C. M. WATSON.

Industrial Dermatitis

SIR,—Dr. Sydney Thomson in his article (*Journal*, May 17, p. 1135) mentions friction (from scratching) as a perpetuating factor in dermatitis. But there is another way in which friction plays a part in dermatitis and it is one which concerns the industrial doctor. Friction is one of the "plurality of causation factors," to use Dr. Thomson's own expression. Some violent agents need no help from friction to cause dermatitis. But most chemicals used in industry are mild in action and need the aid of friction to start a rash. Examples are numerous. Cutting oils do not cause a rash where the oil contaminates the skin, but only where the oil is rubbed into the skin, as when oil-soaked trousers are worn. In fact it seems safe to work with the bare skin if the oil can flow on and off without hindrance or friction. Similarly with mild alkalis.

I can recall much dermatitis from a case-hardening compound. The workplace was thick with charcoal and sodium bicarbonate, but the dermatitis occurred on the backs of the hands, which were used for tamping the substance into case-hardening pots. If a gardening trowel was used the handle was used for the tamping process and no dermatitis was seen, even though the skin became dusty. In the construction of gliders during the last war dermatitis from the resin-glues started on the backs of the fingers because this portion of the skin was rubbed into the resin while inserting tacks or screws into the wood. It did not matter so much that dried resin contaminated other non-friction-bearing areas of skin.

This simple observation sometimes suggests a remedy in that the cure lies in a slight alteration of technique. It entails also recognition that the friction which triggers the rash must perforce also remove a barrier cream.—I am, etc.,

Chester. G. WHITWELL.

Ulceration after B.C.G.

SIR,—Serious complications following B.C.G. vaccination are fortunately rare, but minor local complications are not uncommon. The latter cannot be dismissed as unimportant, however, because they are unpleasant, and a tiresome experience with one child may make parents reluctant to have other members of the family vaccinated. The common local complications are prolonged ulceration at the vaccination site and adenitis in the regional lymph glands. Although lymphadenitis always resolves spontaneously, glands may remain palpable for a very long time and may eventually calcify. If adenitis progresses to abscess formation then healing is usually extremely slow, but recovery can be accelerated by surgical curettage.[1]

In the past it has been common practice to treat persisting B.C.G. ulceration with local application of anti-tuberculous drugs such as para-aminosalicylic acid (P.A.S.) or isoniazid. The response to these drugs is slow, however, and it was therefore thought worth while to search for a more rapidly effective treatment. The ideal local application should be effective against both B.C.G. and secondary pyogenic invaders. It would have added advantage if at the same time it suppressed inflammation and discouraged the formation of unsightly scar tissue. Neomycin is effective against tubercle bacilli,[2] and together with bacitracin forms an antibiotic combination which is topically active against the majority of common pyogenic organisms. Hydrocortisone was selected as the anti-inflammatory agent, and a preparation containing these three drugs, "hydroderm" (hydrocortisone 1%, neomycin sulphate 0.5%, and bacitracin 1,000 units per gramme), was therefore obtained for trial. All patients were vaccinated with 0.1 ml. of Danish vaccine intradermally and were selected for treatment if ulceration was present three months after vaccination and was not showing signs of healing. The hydroderm ointment was applied to the ulcer twice daily on cotton gauze until healing was complete. During the last two

years 20 cases have been treated with very encouraging results. In all instances healing was complete within seven days and there was no relapse. Twelve patients responded dramatically to treatment, their ulcers healing completely within three days.

Many patients develop nothing more than a nodule or small vesicle at the site of B.C.G. vaccination, yet they develop strong tuberculin sensitivity and presumably immunity. If it is also remembered that soon after vaccination there is dissemination of bacilli to the regional lymph glands and more distant sites in the body,[3] it becomes obvious that nothing is to be gained by allowing ulceration to persist at the vaccination site. It is therefore now my practice to treat all B.C.G. ulcers which are present when patients attend for their routine post-vaccination tuberculin test. By doing this patients are relieved of some inconvenience and grounds for criticism of B.C.G. vaccination can be minimized.

I am grateful to Dr. Brian Thompson for permission to publish. My thanks are also due to Messrs Merck, Sharp, and Dohme Ltd. for supplies of hydroderm ointment.

—I am, etc.,

Rickmansworth, Herts. H. R. C. RICHES.

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Rheumatology as a Whole-time Specialty

SIR,—As a British doctor who was obliged to leave the United Kingdom four years ago because rheumatology was not then recognized by the National Health Service as a specialty, I have been very interested to read the correspondence on this subject and to learn that the same state of affairs still exists. There may be arguments for and against the establishment of such a specialty, but the type of doctor best fitted to practise rheumatology is beyond question. In this connexion, the opinion of Drs. Michael E. Fearnley and P. Hume Kendall (*Journal*, May 10, p. 1124) cannot be allowed to pass without comment.

It is generally accepted that the basic treatment of most rheumatic diseases consists of a balanced programme of carefully graded exercises and carefully selected physical therapy. As such, one does not question the ability of the specialist in physical medicine to prescribe and supervise such treatment. It should be realized, however, that the management of most patients suffering from arthritis and rheumatism requires a judicious combination of physical therapy, medical therapy, and not infrequently simple psychotherapy, in addition to the possible use of orthopaedic surgery. The total care and supervision of such a combination of treatment can only be carried out by the doctor trained to treat the patient as a whole, and not the disease or local disability. Such a person is the general physician, or internist as he is called on this side of the Atlantic.

What is more important is that the specialty of rheumatology includes diagnosis in addition to treatment. It cannot be too strongly emphasized that aches and pains often ascribed by the patient to "rheumatism" may be the presenting symptoms of a whole variety of internal disorders. The so-called collagen or connective-tissue diseases, generalized carcinomatosis (primary or secondary), alimentary disorders (chronic ulcerative colitis, intestinal lipodystrophy), lymphomas and granulomas (sarcoidosis) are but a few examples of this. It is the internist who, when confronted with a patient complaining of pains in the joints or soft tissues, has to consider all these possibilities. By taking a careful history and carrying out a thorough physical examination, he arrives at a tentative diagnosis. The internist deals with the whole of medicine, of which rheumatology is but one branch, and one cannot practise rheumatology without primarily being an internist. There would therefore seem to be an urgent need to establish rheumatology as an important sub-specialty of internal medicine, thus bringing it into line with cardiology, neurology, etc. It is in this manner that rheumatology is practised in Canada and the United States, where arthritis clinics and departments are staffed by internists. Physical therapy, where indicated, is referred to the "physiatrist" (physical medicine specialist), but the overall treatment, care, and diagnosis rests with the internist. The specialist in physical medicine must, of necessity, play an important part in the treatment of the rheumatic diseases, but to state that physical medicine is "recognized by the majority as providing the ideal specialty" to deal with these diseases is misleading, and cannot be accepted.—I am, etc.,

Windsor, Ontario, Canada. L. MANDEL.

Acute Appendicitis

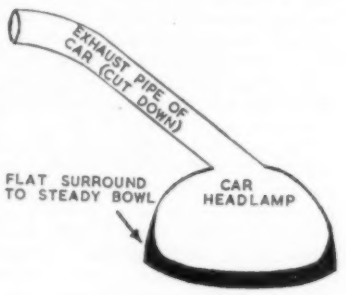
SIR,—I was very interested to read the article by Mr. J. A. Campbell and Mr. D. C. McPhail on acute appendicitis (*Journal*, April 12, p. 852). It is a review of the clinical signs and symptoms of this disease. I feel, however, that a discussion of the findings of rectal examination and white cell count would have added much to the paper. Both of these things are essential to the diagnosis of appendicitis.

May I take this opportunity to mention how much I enjoy reading the *Journal*?—I am, etc.,

Montreal. M.-G. STEGEN.

Urinals for Multiple Sclerosis Patients

SIR,—Having been stricken with multiple sclerosis I would like to describe two simple devices which have helped very greatly in solving the problem—a considerable one—which arises from complete lack of control of one's urinary functions. As the wearing of a rubber urinal had proved a constant trouble from soreness caused by the straps and leakages due to lack of a perfect fit, my doctor and Mr. Gurney, of Messrs. Colliver - Fisher Ltd., devised a urinal (see diagram) which, when one is in an armchair clothed in pyjama trousers and a rug over one, completely solves the problem without needing emptying for periods of up to 10 hours at least. The gadget is made from a car exhaust pipe suitably bent, soldered into a car head-lamp case which has had the glass replaced by metal, again soldered on.



The second device consists of the mere addition of a piece of car radiator tubing which fits tightly into the neck of the ordinary plastic urinal. The purpose of the tubing is to extend the neck of the urinal so that the urinal can be placed at one's side in bed—often necessary when legs are having spasms.

I hope that these ideas may benefit some of my fellow sufferers from this wretched complaint.—I am, etc.,

Northwood, Middlesex. G. E. G. DEVONSHIRE.

Pseudo-medical Advertising

SIR,—Is it not high time that the members of our profession, and particularly the B.M.A., came out strongly against the present spate of pernicious pseudo-medical advertising which daily screams at us from newspapers, placards, and television screens, telling us that we are One Degree Under; that we need this to give us deep relaxing sleep and thus solve all our psychosocial problems, that unless we use that product our children's cerebral cortexes will never put on the spurt needed to pass the 11+, etc., etc., *ad nauseam*? These collections of half-truths, downright falsehoods, and

jargonized dishing-up of old wives' tales are, in my opinion, causing quite an appreciable increase in the minor psychiatric illnesses suffered by the populace.

One feels off-colour, sickly, and grumpy with the children. Unless one immediately takes large rations of "X," a product of no therapeutic value at all unless one has been adrift on a raft foodless for a fortnight, one's husband will instantly pay attention to a pretty girl over the road, or a underling will win promotion over one's head, and so on. Who has not seen the patient with a severe anxiety state, or an early pernicious anaemia, who when asked why he or she had not come for advice earlier, says, "Well, doctor, I've been on so-and-so for three weeks, it's supposed to be so good for this sort of thing, isn't it?" Who says so?—the Telly.

If the B.M.A. and doctors generally united in attacking these advertisements whenever possible and took steps to try to educate patients away from these useless products, not only would medical good be done, but a waste of money, which must amount to millions in a year, be avoided.—I am, etc.,

Linton on Ouse, Yorks. R. E. DAWSON.

I.Q. and Response to Group Psychotherapy

SIR,—Some of your readers might be interested in a comparison I have recently made between the Stanford Revised Binet I.Q. of mental defectives and their response to group psychotherapy. I took as samples 14 males and 17 females from 120 patients who had, at one time or another, participated in group psychotherapy. In 50% the rank orders of the I.Q. and the response to group psychotherapy were equal. As part of the group psychotherapy was devoted to the "draw-a-person" test, one could perhaps say that this test is a fairly good complementary method of assessment.—I am, etc.,

Prudhoe-on-Tyne. A. D. HELLER.

Prevention of Lung Cancer

SIR,—Tobacco consumption in England and Wales last year went up 4.8 million lb. (2.18 million kg.) and reached the record figure of 304.3 million lb. (138 million kg.).[1]

In its statement on "Tobacco Smoking and Cancer of the Lung"[2] the Medical Research Council accepted the evidence associating smoking with a major part of the increase in lung cancer. This was tantamount to accepting the view that a major part of the epidemic of lung cancer now upon us is readily preventable because tobacco-smoking is readily preventable—it is no more difficult to prevent than opium- or hashish- smoking (which we now prevent), and large numbers of smokers stop smoking voluntarily. Yet the M.R.C. made no recommendations in this statement for preventing lung cancer by stopping people smoking. They were thus guilty, it seems to me, of a grave act of omission. They followed the precedent established by their chief investigators on this subject, Dr. R. Doll and Professor A. Bradford Hill, of merely setting out the evidence and their conclusions, which carried an implied warning for smokers. But tobacco is far too powerful a drug of addiction to be abandoned, except by a small minority of smokers, in response to mere implied warnings about a remote risk—as the tobacco consumption figures testify. Such warnings have often, indeed, an immunizing effect. Many smokers have acquired such a degree of immunity to fear of lung cancer, as a result of repeated inadequate warnings over the past seven years, that they are quite unscarable: their protective emotion, fear, no longer fulfils its normal function where lung cancer is concerned.

In the absence of any recommendations from the M.R.C., the Government, a lay body which consists mainly of smokers, put in hand measures of its own devising for ending the epidemic of lung cancer. These are a complete farce: the Government merely passed the buck to the local authorities. Cancer of the lung is not, of course, a local but a national problem, and only the national Government has the power to deal with it effectively.

The nation's smoking could be cured almost overnight and the great bulk of lung cancer prevented by a national anti-smoking campaign followed by legislation aimed at doing away with tobacco-smoking within a matter of months. The campaign would consist of educational talks at peak listening times on T.V. and sound radio on the effects of tobacco smoking on the human organism. Blunt warnings about the damage smoking does, coupled with firm injunctions to smokers to stop smoking, could be interposed from time to time between programmes. Everything connected with the campaign should be in the hands of non-smokers, since smokers are obviously pro-smoking, and anti-smoking words on their lips must be hypocritical, however much smokers may protest their sincerity. There is no objection to frightening smokers about the effects of smoking just as there is none to frightening children about the effects of fire.

The economic effects of the nation's stopping smoking would be a problem primarily for the Chancellor of the Exchequer. For too long have successive Chancellors shamelessly exploited the smoker's craving for tobacco to extort from him enormous sums in the form of taxation.—I am, etc.,

Wallasey. LENNOX JOHNSTON,
President, National Society of Non-smokers.

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Recognition of Intoxication

SIR,—Your annotation on the recognition of intoxication (*Journal*, May 31 p. 1293) delighted and surprised me. As one concerned for over twenty years in the practice and teaching of forensic medicine, it is somewhat distressing to note the tendency in the less enlightened universities to reduce the teaching in forensic medicine and, in fact, in some cases to eliminate the subject from the list of professional examinations altogether. Perhaps your annotation may be interpreted as an indication of a reawakening of the university authorities to the usefulness of the subject.

A professional reputation may be marred in a few minutes by a trouncing in the witness-box administered to one improperly prepared, and, apart from that aspect of the matter altogether, the increase in civil litigation involving the medical profession must surely call for instruction of the undergraduate in his ethical and legal obligations. While little harm may be done if a misdiagnosis is made of some rare chronic malady, most medico-legal situations demand action and decision at once. A wrong decision may have disastrous effects on the doctor, the patient, or both. I am sure that practical instruction and examination in these aspects of the subject which concern the general practitioner are essential if properly educated doctors are to be turned out. Admittedly, some aspects of the subject are the concern only of those specializing in its practice, but many are basic necessities for practitioners in all spheres, and obvious ignorance of the functions of the coroner, of death certification, of certification of the insane, as well as of the regulations governing cremation may seriously damage the practitioner's reputation in the eyes of his patients.—I am, etc.,

Sheffield, 10. GILBERT FORBES.

POINTS FROM LETTERS

Stress-Induced Distress

Dr. GWENDOLINE M. LANGHAM-HOBART (Paisley) writes: With reference to your special correspondent's report on the conference on "The Nature of Stress Disorders" (*Journal*, May 17, p. 1173), it would appear that the concept of "stress-induced distress" requires clarification. . . . It might be profitable to imagine that, just as an adequate stimulus is thought to produce a specific reaction and overstimulation of any sensory modality may cause pain, so adequate stress elicits function and undue stress, which is distress, results in dysfunction, and may later produce disease. There is also a sociological implication within this framework.

Obituary

J. C. MIDDLETON, M.B., Ch.B., B.Sc., F.R.F.P.S.

Dr. J. C. Middleton, honorary consulting physician to the Glasgow Royal Infirmary, died on May 30, aged 74.

John Clark Middleton, the son of a schoolmaster, was born in Glasgow on June 12, 1883. From Whitehill School he went on to Glasgow University, graduating in arts before taking the degrees of M.B., Ch.B. (with honours) in 1907. He also took the B.Sc. (public health) after having taken the same degree in general science some years earlier. After graduation he held the usual house appointments at the Western Infirmary, Glasgow, and the McCann research scholarship in medicine. He then went into general practice and combined this with the post of assistant to the late Professor Ralph Stockman, professor of materia medica and therapeutics in the University of Glasgow. In 1911, also, he joined the staff of the Royal Infirmary as extra dispensary physician. Appointed physician in charge of wards, in 1926, he held that post until his retirement in 1943. As a clinical teacher and examiner he was known to hundreds of undergraduates, and he brought to his teaching a wealth of experience gathered in general practice, together with a profound scientific knowledge. He was elected F.R.F.P.S. in 1920.

J. W. M. writes: Dr. J. C. Middleton was well known to Scottish medical circles. Although he spent a large proportion of his professional life as a pharmacologist and a teacher of materia medica, it was as a diagnostician that he is remembered by most. His ability in this field has become almost a legend, and many tales of the uncanny accuracy of his judgment are told by his students and his staff. "Jock" Middleton, as he was known to many, was an extremely shy man, and this was mistaken, by those who did not know him well, for aloofness. Those who worked for him not only respected him but had a real affection for him, and his residents for many years before his retiral from the Royal Infirmary met annually as members of an exclusive "J. C. M." club, at which their chief presided. Only those who were taught by and who worked with Dr. Middleton can be truly aware of his greatness as a physician and of the magnitude of the loss occasioned by his death.

Sir DARCY COWAN, M.B., F.R.A.C.P.

Sir Darcy Cowan, an authority on respiratory diseases and honorary consulting physician to the Royal Adelaide Hospital, died earlier this month. He was 72 years of age.

Darcy Rivers Warren Cowan was born on August 8, 1885, the sixth son of James Cowan, a former member of the House of Assembly of South Australia. After leaving Prince Alfred College he studied medicine at Adelaide University, and graduated M.B., B.S. in 1908. During the first world war he served as a lieutenant in the R.A.M.C. in 1914–15 and as a captain in the A.A.M.C. from 1916 to 1918. After the war he settled in practice in Adelaide, and from 1924 to 1935 was honorary physician to the Royal Adelaide Hospital, being elected honorary consulting physician in 1938. From the latter year until 1950 he was physician in charge of the chest clinic at the hospital. Other appointments he held were those of medical director of the South Australian Tuberculosis Association and president of the Northcote Home, both from 1943 to 1955, and chairman of the Kalyra Sanatorium from 1950 to 1955. He was honorary secretary of the National Association for the Prevention of Tuberculosis in Australia from 1948 to 1955. He was elected a foundation Fellow of the Royal Australasian College of Physicians in 1938, and a Fellow of the American College of Chest Physicians in 1946. A member of the British Medical Association for nearly fifty years, he was president of the South Australian Branch from 1935 to 1937. He was created a knight in the 1955 Birthday Honours. As a young man Sir Darcy Cowan excelled at ball games, and represented his university at football, lacrosse, and lawn tennis. He was honorary organizer of the Davis Cup challenge rounds in 1952 and 1956. He married Miss Effie Hewitt Cox in 1910.

A. G. BRAND, M.B., Ch.B.

Dr. A. G. Brand, who was in general practice at Ayr for nearly forty years, and radiologist to Ayr County Hospital for much of that time, died on June 2. He was 67 years of age.

Alexander George Brand was born on March 30, 1891, and was educated at the Old Collegiate School, Glasgow, and Morrison's Academy, Crieff. He then studied medicine at Glasgow University, and, after graduating M.B., Ch.B. in 1916, served as a captain in the R.A.M.C. during the remainder of the first world war. He settled in general practice at Ayr in 1919, and seven years later was appointed radiologist to Ayr County Hospital, a post he still held at the time of his death.

A colleague writes: By the death of Dr. Brand the medical profession has lost a member who successfully blended a deep interest in general practice and radiology with intense interest in the arts. In 1930 he brought together local musicians to form a small orchestra to supply incidental music to many plays publicly presented in Ayr. From that date his time was filled, outside his practice, with unflagging interest in the Ayrshire Philharmonic Opera Society, the Ayr Amateur Players, the Ayr Fort Players, and in the Ayr Compass Club. Dr. Brand was for fourteen years honorary conductor of the Ayr Amateur Orchestra. It is indeed hard adequately to outline the many artistic and cultural interests he so untiringly served, and there are many who owe much of their subsequent success to his advice and encouragement in the world of art and of music. A life of tireless devotion to medicine, music, and art has ended, and we mourn his passing.

L. C. WALKER, M.B., B.Chir.

Dr. L. C. Walker, who was in general practice at Malton, Yorkshire, for over forty years, died suddenly at his home there on May 31 after having been in indifferent health since his retirement in 1956. He was 73 years of age.

The son of Dr. J. B. Walker and a nephew of Sir William Broadbent, Physician Extraordinary to Queen Victoria and King Edward VII, Lawrence Cecil Walker was born near Huddersfield on April 29, 1885. Educated at Oundle and at Christ's College, Cambridge, he went on to St. Mary's Hospital medical school to receive his clinical training. He qualified M.R.C.S., L.R.C.P. in 1912, and in the following year settled in Malton as successor to the late Dr. Ernest Colby, who was himself a fine example of the general-practitioner surgeon of those days. Dr. Walker quickly gained a reputation as a surgeon in the local cottage hospital, which received patients from a wide area. With the outbreak of war in 1914 auxiliary convalescent homes and hospitals sprang up in the neighbourhood, and he played an active part on the staffs of these. In 1925 he obtained the degrees of M.B., B.Chir.

F. L. A. H. writes: During the first world war Dr. L. C. Walker suffered an attack of rheumatic fever which was eventually to leave him with an impaired heart: in addition, he became inflicted with a gradually increasing deafness, which he bore with remarkable equanimity but which in later years must have been a severe handicap and trial to him. In 1925, in company with other local practitioners

and a very enlightened and energetic house committee, he played an important part in providing the neighbourhood with a model cottage hospital of twenty beds, with an up-to-date operating theatre and facilities for radiography. For the rest of his life he gave the hospital devoted and unstinted service as surgeon and, later, as chairman of the house committee and as a member of the Scarborough group management committee. The Leeds Regional Hospital Board recognized his ability and services by granting him—a general practitioner—full consultant status on the inception of the National Health Service, a position he held until his retirement in 1956.

Dr. Walker was also prominent in local government circles, being medical officer of health of one urban and two rural district councils for many years, during which time many housing estates and water and sewage schemes were completed. In 1932 Malton suffered a disastrous epidemic of typhoid fever. As medical officer of health, Dr. Walker was faced with a massive task, from which he did not flinch. With supreme energy and wisdom he and others in the town produced effective measures for combating the disease and dealing with nearly 250 cases.

In his early years he was actively connected with the local organizations of the British Red Cross Society, and he was also instrumental in starting an infant welfare centre. Despite so much public activity he still found time to be the old-time general practitioner to a large number of people in all stations of life. His kindliness, steadfastness, and imperturbability will always be remembered by his patients as the foundation upon which they built their faith and confidence in him in times of trouble. And it is these attributes that we, who were privileged to know him and work with him, will always associate with his memory. He he leaves a widow, two sons, and a daughter, to whom all will wish to extend their sympathy.

E. S. A. CRAWFORD, M.B., B.Ch.

Dr. E. S. A. Crawford, who had been in practice at Sidcup, Kent, for the last twenty years, and before that at Swanley for some ten years, died suddenly at his home at Sidcup on May 25, aged 58.

Edward Sydney Atkinson Crawford was born on May 16, 1900, the son of the late Dr. R. A. Crawford, and was educated at the Royal School, Dungannon, and at Trinity College, Dublin. After graduating M.B., B.Ch. from Dublin University in 1925, he held house appointments at the Nottingham General Hospital and the Kent and Canterbury Hospital, and during this time became particularly interested in surgery. In 1928 he joined his father and twin brother, the late Dr. R. R. Dawson Crawford, in practice at Swanley, taking over most of the surgical work. The cottage hospital near Sidcup was where he did his operative work, and in 1937 he moved to that district so that he could be nearer the hospital. His heart was in that work, and it was a great grief to him when, after the introduction of the National Health Service, this was denied him. He joined the R.A.M.C. in February, 1940, and served in England for two years, first with a field ambulance and then as a surgical specialist, with the rank of major, at a base hospital. During the last three years of the second world war he served in Gibraltar, Africa, India, and Burma, attaining the rank of lieutenant-colonel. Late in 1945 he had a severe gastric haemorrhage and was sent home. From then onwards he suffered a great deal of ill-health, and finally, last February, he had pneumonia complicating a severe attack of influenza, never recovering sufficiently to be able to work again. His death terminated a career of devoted service as a doctor. Carrying on the work begun by their father at Swanley at the end of the last century, Dr. Sydney, as he was popularly called, and his brother gained the deep affection of the people in the district.

In 1928 he married Dr. Marie L. P. Goetze and had two sons, the younger of whom, Dr. R. A. Crawford, obtained his medical degrees at London University last year.

Lord WEBB-JOHNSON, G.C.V.O., C.B.E., D.S.O., Hon.LL.D., M.B., Ch.B., F.R.C.S.

The obituary of Lord Webb-Johnson was printed in the *Journal* of June 7 (p. 1357).

Mr. DAVID H. PATEY writes: Much has naturally been written of "Webb-J." as an organizer whose outstanding vision and accomplishments exercised such a profound influence on all the institutions he served. Less has been written of him as a doctor, and the following story of what must have been his last consultation may help to fill in the picture of the surgeon and the man. It recently fell to my lot to take over from Professor Windeyer the care of a lady on whom Webb-J. had performed a radical removal of the breast 14 years previously. She had done very well, but had developed a second primary in the remaining breast. We informed Webb-J., but, knowing he was ill, we did not expect a reply. Not only did he reply by return with a typical personally written letter, but he expressed a wish to see the patient. Accordingly, only a few weeks before he died, the patient and I went round to see him. He was obviously very ill, and the consultation took place in his bedroom though he had got up and was dressed for it. He confirmed the advice of further surgery, and the consultation gave much help and comfort to the patient. After the operation I wrote to tell him the findings, and this he acknowledged by return with another personally written letter. I promised to let him have the full pathological report, but I did not get it until my return from a short Whitsun holiday, and by then there was no need to tell him.

Mr. R. W. RAVEN writes: May I add a tribute to the memory of the late Lord Webb-Johnson on behalf of all who are connected with the Royal Medical Foundation of Epsom College. Lord Webb-Johnson succeeded the late Viscount Leverhulme as our president in 1951, and held this office until his death. During these seven years important developments have taken place in the College; it is fortunate that we had the benefit of his wise counsel in our affairs and the privilege of his stimulating presence with us on so many occasions. How effectively he intervened when this was necessary and how apposite his remarks on any problem under discussion. It was due to his inspiration that plans for a centenary building programme were finally agreed and an appeal for funds to implement our plans was launched; indeed, with his characteristic generosity he inaugurated this appeal with a large personal gift. Our sorrow is deepened by the reflection that we are denied his presence when the new school house is officially opened on near-approaching Founder's Day. We loved this happy man with the tranquil mind and merry heart.

J. T. DUNCAN, F.R.C.S.I., D.T.M.&H.

Sir PHILIP MANSON-BAHR writes: I would very much appreciate it if you could add this tribute of mine to your obituary (June 14, p. 1420) of my old friend Duncan. Posterity will no doubt award Duncan the distinction which he deserves. Of all the friends I have known who have devoted themselves to the study of tropical diseases and their parasites, I think that he stood out by his honesty of purpose and single-mindedness. His was the hard way. Time after time during his career in Malaya and in London he turned down offers of a lucrative practice to give all his time and attention to research. He did an enormous amount of scientific work on bacteriology and pathology, all of a high order, but he will best be remembered for the great service he gave to tropical medicine in putting the much neglected subject of mycology on the map. When he took up fungus diseases seriously he found the nomenclature in a chaotic state. He put that straight and he also performed an enormous amount of work in describing the normal morphology of the pathogenic mycoses and linking it up with clinical manifestations. He was the first to insist on the elevation of the study of mycology to a place in the tropical medicine curriculum

and in obtaining recognition from London University. It is very much hoped that the standard laboratory which he founded will continue in his name, and that the book on medical mycology to which he devoted his latter years will soon see the light of day.

Medical Notes in Parliament

ANOMALIES IN REGISTRATION

The Medical Act, 1956, Amendment Bill, which Mr. J. B. HYND (Sheffield, Attercliffe, Lab.) was given leave to introduce on June 11, has the support of the Government, the various Ministries, the General Medical Council, and the B.M.A. Its purpose is to remove defects and anomalies which eight years' experience has shown to exist in some parts of the 1950 Act, although its title refers to the consolidation measure passed in 1956.

The amendments it is sought to make relate to the experience required for full registration and to applications for provisional registration, and to fees, expenses, and allowances of the G.M.C. Mr. Hynd, who was a member of the body when the 1950 Act was passed, said that a number of cases had come to notice which showed that the wording of the Act had proved anomalous, and had resulted in serious injustices and a cumbersome and complicated procedure which it was the desire of everyone concerned to avoid.

Two groups were affected by the existing provisions relating to full registration. The first were those who qualified before 1953 but for various reasons did not apply for full registration; for example, doctors who qualified before or during the war and went abroad with the Forces, and spent many years in practice, including hospital experience, or went abroad on medical missionary service and had similar experience. On their return to this country they found that they could not obtain full registration until they had undertaken another year's internship training in a hospital; and because of this technicality they had been unable, in spite of having all the training and experience necessary, to obtain posts open to them, and for which their services were required, until they had undergone this internship.

The second group were foreign or Commonwealth doctors with diplomas not recognized for registration in this country. Whatever their previous qualifications or experience they must pass a British examination and have a British diploma. Then they found that they could not be registered because they had still to do 12 months in a hospital, irrespective of their previous experience. The holder of a recognized foreign or Commonwealth diploma could be placed on the *Register* immediately if he satisfied the G.M.C. that he had the full hospital experience required. The Bill would apply this practice to all foreign and Commonwealth doctors, and to doctors registered before 1953 who could produce evidence that they had at least as much hospital experience as was required from a newly qualified doctor for registration.

Provisional Registration

A doctor who had applied for provisional registration so that he could undertake his 12 months' internship after the qualifying examination, and who had obtained a job in a hospital, must first produce a certificate of selection for employment in the hospital, which must then be submitted to his examining body, who must then check with the hospital, check his qualifications, and issue a further certificate. About 2,000 cases a year were dealt with. The G.M.C. and other bodies concerned would confirm that there were considerable delays involved. There might be many hundreds of doctors practising for days or even weeks in hospitals quite illegally while waiting for the formal notification that they had been registered. The provision was largely useless. It was cumbersome and embarrassing to everybody, and did not provide an effective check, as it applied only to the first post. It would be generally agreed that the purely technical provisions involving the time factor between the certificate of employment and provisional registration should be eliminated and the authority left in the hands of the General Medical Council, as was done satisfactorily before 1950.

The Bill also amended the Schedule of the 1950 Act, which required the fees and expenses of members of the G.M.C. and its branch councils should be such as might be decided by the Council with the approval of the Treasury. This might have been necessary 100 years ago, when the Council was first set up as an experimental body; but it no longer meant anything, because in any case there were no public funds in the Council's budget.

On June 13 the Bill was read a second time, and committed to a committee of the whole House.

INSANITY AND DIVORCE

When the Divorce (Insanity and Desertion) Bill* was considered in committee by the House of Lords on June 12, Lord DENNING moved a new clause providing that in a petition for divorce the court might hold that the respondent had treated the petitioner with cruelty notwithstanding that a disease of the mind prevented his acts from amounting to cruelty, if the evidence was such that the court would have so held apart from the disease.

He said the amendment was designed to give effect to a unanimous decision of the Royal Commission. A mental disease operated insidiously, unrecognized, progressively, until there was some catastrophe when it became apparent to everyone. In the earlier time the husband might well have been guilty of cruelty and have wrecked the marriage. Was the wife, because he was afterwards found to be insane, not to have a remedy in divorce?

Lord MERRIMAN, president of the Divorce Division, pointed out that the courts up to now had supported the opposite view. The question was whether the offence of treating with cruelty could occur at all if the acts complained of were committed at a time and in circumstances when the McNaughton Rules applied—if a man could prove that by a defect of the reason, owing to a disease of the mind, he either did not know what he was doing or did not know that it was wrong. The Court of Appeal, after some hesitation, had recently held in three cases that, if the aggressor could bring himself within the McNaughton Rules, that applied as a defence to a charge of cruelty just as it would to a criminal charge. If the test was that the cruelty must be aimed at the victim, how could an insane man "aim" his acts at his spouse? The previous day he had discussed the matter with all the judges of the Division he could see, and there was a remarkable division of opinion about the expediency of the new clause. It would be a drastic change, but if Parliament ordained it the judges would carry it out with all loyalty.

The LORD CHANCELLOR asked for further time for himself and the Government to consider the question, and on this assurance the new clause was withdrawn.

EXTENSION OF LEGAL ADVICE

The LORD CHANCELLOR announced on June 12 that the Law Society had made proposals for implementing section 7 of the Legal Aid and Advice Act, providing in substance for the giving of oral advice by solicitors in ordinary practice for a fee paid out of the Legal Aid Fund. It appeared to the Government that such a scheme would be more satisfactory than the employment of salaried legal advisers, and they were prepared to adopt it. If, as they hoped, sufficient solicitors indicated their willingness to undertake this work, it was intended to bring section 7 into force towards the end of this financial year. Similar arrangements would be made under the Scottish Act. It was expected that section 5, the remaining section dealing with legal aid, would be brought into force later next year.

*See *British Medical Journal*, May 31, p. 1306, for report of the Bill's second reading in the Commons.

ANSWERS TO QUESTIONS

U.N. Inquiry on Nuclear Radiation

Mr. K. ZILLIACUS (Manchester, Gorton, Lab.) asked the Prime Minister on June 10 whether, in view of the finding of the United Nations Committee to the effect that the nuclear test explosions that had already taken place would produce anything up to 120,000 cases of major genetic defects a year, he would suspend British tests and agree to negotiate a treaty banning tests immediately.

Mr. R. A. BUTLER, Home Secretary and Lord Privy Seal, who replied, said the draft report of the U.N. Scientific Committee on Radiation was still under consideration by the committee. The House would be well advised not to take account of speculations on what the report might say, but await its completion. He understood this was likely to be about July 1.

Diagnostic Radiology

Captain R. A. PILKINGTON (Poole, Con.) asked, in view of the fact that medical diagnostic radiology was responsible for about 22% of natural radiation, and nuclear fall-out from hydrogen bombs was responsible for about 1%, what representations he had received for mitigating the possible dangers of diagnostic radiology. Mr. BUTLER pointed out that the Medical Research Council's report, *Hazards to Man of Nuclear and Allied Radiations*,* recommended a review of the present practice in diagnostic radiology, and a committee under the chairmanship of Lord Adrian was engaged on such a review.

Physician Superintendents' Fees

Mr. R. BODY (Billericay, Con.) asked the Minister of Health how far physician superintendents of mental hospitals were entitled under his regulations to charge any fee they chose to nominate when they were asked to swear an affidavit that a patient had been under their care and when that affidavit was essential to divorce proceedings on the ground of insanity. Mr. D. WALKER-SMITH replied that this was not part of the hospital and specialist services provided under the National Health Service Acts, and the question of a fee was one for the parties concerned.

Wessex Hospital Region Next April

The MINISTER OF HEALTH announced in a written reply on June 13 his decision that it would be possible to set up a separate Wessex Regional Hospital Board for the South-west Metropolitan Region on April 1 next year. He added that he was taking the necessary steps to bring the new region and the regional hospital board into being on that date.

Inquiry into Drug Addiction

The MINISTER OF HEALTH, replying to Sir HUGH LINSTEAD (Putney, Con.) on June 16, stated that he had appointed a committee, under the chairmanship of Sir Russell Brain,

"To review in the light of more recent developments the advice given by the Departmental Committee on Morphine and Heroin Addiction in 1926; to consider whether any revised advice should also cover other drugs liable to produce addiction or to be habit-forming; to consider whether there is a medical need to provide special, including institutional, treatment, outside the resources already available, for persons addicted to drugs; and to make recommendations, including proposals for any administrative measures that seem expedient, to the Minister of Health and the Secretary of State for Scotland."

The members of the Committee are: Mr. Lawrence Abel, Professor D. M. Dunlop, Mr. Donald W. Hudson, Professor A. D. Macdonald, Dr. A. H. Macklin, Dr. S. Noy Scott, Dr. M. A. Partridge, with Dr. Roy Goulding and Mr. W. G. Honnor as joint secretaries.

*1956, H.M.S.O., London.

Poliomyelitis Vaccinations

Mr. B. JANNER (Leicester, North-west, Lab.) asked the Minister of Health when he anticipated there would be enough vaccine against poliomyelitis for all persons at present registered to have the full three vaccinations.

Mr. WALKER-SMITH stated that by April 30, the latest date for which detailed information was available, over three million persons in Great Britain had been vaccinated with two injections, just over two and a half million were awaiting vaccination, and a further half-million were awaiting their second injection. On that date the local health authorities held one million doses of vaccine and they had since received over five million more. This was more than sufficient to complete the vaccination with two doses of all persons registered by April 30 if they were willing to accept the type of vaccine available. Registration was a continuing process, and further supplies of vaccine were being distributed from time to time to keep pace with new registrations. He could not at present make any statement in regard to extending the offer of vaccination to other priority groups or about the giving of third doses.

Dr. EDITH SUMMERSKILL (Warrington, Lab.) asked what proportion of those registered had refused vaccination because they could not have the type they preferred. Mr. WALKER-SMITH said the response to the offer of Salk vaccine varied with the areas concerned. In general, parents were accepting the advice of the Medical Research Council and having their children vaccinated with the vaccine available in the area, rather than let them go unvaccinated over this summer season.

Report on Prescribing

Mr. JOHN ARBUTHNOT (Dover, Con.) asked when it was proposed to publish the interim report from the Committee on Prescribing under the chairmanship of Sir Henry Hinchliffe. Mr. WALKER-SMITH: On June 23. I am already in consultation with the British Medical Association and other organizations as a preliminary to deciding how far the recommendations of the Committee can be put into effect.

Cancer Research

Sir FRANK MEDLICOTT (Norfolk, Central, Ind.) asked what exchange of information and research into the causes of cancer took place between the appropriate official authorities and organizations in the United Kingdom and the Union of Soviet Socialist Republics. Mr. WALKER-SMITH stated that experience had proved that the most valuable international scientific liaison was that which took place on an informal and individual basis, and such communication between the Union of Soviet Socialist Republics and this country had recently shown signs of increasing. The attendance of a number of Russian experts at the International Cancer Congress in London next month would provide a further opportunity for useful contacts to be made in this field of research.

Princess Louise Hospital Decision

The decision of the Minister of Health on the future use of the Princess Louise (Kensington) Hospital for Children, announced in the House of Lords on June 16, is that he would be justified in approving the temporary use of two wards for maternity patients but that he should not approve the long-term use of the hospital for adults. This is to be reviewed again towards the end of the period of temporary use for maternity purposes.

Lord STRATHCLYDE, Minister of State, Scottish Office, who announced the decision, recalled that the proposal made by the governors of St. Mary's Hospital was twofold: that for a temporary period during the adaptations of the maternity unit at St. Mary's two wards at the Princess Louise Hospital should be used for maternity purposes; and that thereafter the hospital should become a hospital for adults.

He said the Minister had considered this proposal in the light of the views of the hospital authorities and others

concerned, including the University of London and St. Mary's Medical School. He had also had regard to the terms of a restrictive covenant attaching to the land on which the Princess Louise Hospital stood, which limited the use of the building to that of a hospital for children with maternity wards, and to his obligations under the Health Service Act.

He added, in answer to Lord Balfour of Burleigh, that 39 cots in the two wards to be converted were to be removed, and there would be 20 beds for mothers. It was expected that these would be used for about two years after the work of adaptation, to be begun this year, had been completed.

Medico-Legal

PSYCHOPATHOLOGY OF ARSON

[FROM AN EXPERT IN FORENSIC PSYCHIATRY]

On the basis of calculations made from the *Criminal Statistics for England and Wales* published in the last five years,[1] it appears that some 250 persons are each year convicted of arson. The ratio of males to females is 21.5 to 1, and the ratio of those over 21 to those under 21 is 0.3 to 1; the corresponding figures for conviction in all indictable crime are 6.8 to 1 and 1.2 to 1 respectively. Some 75% of the convictions for arson are therefore recorded against minors, 51% of the total being under 14 years of age (52% of males and 25% of females). From this age-group (the under-fourteens) the incidence among males falls rapidly to 17 years and thereafter more gradually to old age, with the exception of a slight rise in the 25–30 age-group. The incidence among females falls less steeply to 30 years, then rises in the 30–40 age-group and even more sharply in the 40–50 age-group, thereafter falling progressively to old age.

Arson therefore seems particularly to be associated with male youths. This and the fact that those who commit arson are generally people of limited intelligence is also the experience elsewhere. The rising incidence in the women of 30–50 is presumably related to the menopause and is paralleled to some extent in crime generally.

Aetiology

Wilhelm Stekel,[2] in his classical monograph on pyromania (a term criticized by East[3] as archaic), accords to it a special sexual significance—"... a symbolic solution of his conflict between instinct and reality ... unrequited love is the most common motive of arson." He believed that the repressed sexual wishes might be normal or abnormal. He pointed out that the aggression apparently directed against the owner of the fired property might in reality be directed against the culprit's parents—"... they shall see to what their lack of heart has led ... they are responsible for everything." Fenichel[4] believed that the pleasure in starting a fire might become the indispensable condition for sexual enjoyment—the so-called incendiary perversion. These authors contend that the motives usually advanced for the crime are purely superficial and cover the real motives, which are almost invariably sexual and which may be discovered by analysis.

Other investigators[5,6,7] emphasize the frequency of less deep-seated reasons such as resentment, nostalgia, and mischief, and do not feel the need to invoke a sexual interpretation. Nor are they content readily to condone a plea of irresistible impulse, which, they feel, is often brought forward to shield a person from the legal consequences of an act for which he may be rightly responsible.[8] Arson is only very rarely a symptom of an obsessive compulsive neurosis.[9,9] As Cleckley[10] declares, the distinction between compulsive acts of caution and "compulsive" antisocial acts is a fundamental one and brings out a distinction not only of degree but also of quality. Neither need it be assumed in the individual case that the commission of arson indicates psychopathy. Not only may the action be a quite specific one, but the lack of general moral sense and wisdom and the callousness of the true psychopath may not be in evidence. According to Kretschmer,[11] arson is an example of what he calls a short-circuit action, "in which affective impulses elude the total personality and are directly translated into action."

Apart from the cases where arson is the primary and sole phenomenon, there are those where it is symptomatic of an underlying psychosis. In the presence of signs of withdrawal and a very flimsy motivation, schizophrenia must always be considered. Arson may also be committed in the course of epilepsy, depression, senility, alcoholism, and mental defect. Clearly the action may proceed more from curiosity and stupidity than from malice in some of these conditions. Where therefore there is any reasonable doubt about the mental condition of the accused or the motives for his behaviour it will be reasonable to insist on a full clinical and psychological examination.

Prognosis

Where the arson is a symptom of underlying psychosis the treatment and prognosis will be that of the psychosis. Where it occurs in a non-psychotic child the long-term prognosis would appear to be quite favourable, the likelihood of recurrence diminishing rapidly with the passing years. A recurrence at the menopause is presumably a theoretical possibility where girls are concerned. In these children there appears to be no reason to depart from the usual methods of investigation and treatment of any behaviour disorder at this age. With Burt's[12] concept in mind of the multiple causation of delinquent behaviour—physical, mental, and social—treatment should embrace a comprehensive approach to the whole family, socially and psychologically. The presence of a serious degree of mental defect, especially if combined with psychopathic personality traits, would of course make for an ominous prognosis, and such children may require institutional treatment.[8,13]

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THE PERIOD OF GESTATION

[FROM OUR LEGAL CORRESPONDENT]

In December, 1952, Mr. and Mrs. Burgess were married in Kenya, where they had been living together as man and wife for some seven years. Towards the end of 1954 Mrs. Burgess, who said that her health was seriously affected by the Kenya hot season and who was alarmed by the trouble with the Mau Mau, came to England. On April 22, 1955, Mr. Burgess came to England and spent his time with his wife until his return to Kenya on May 14, 1955. Intercourse took place between them on the night of April 22 or 23.

When Mr. Burgess returned to Kenya his wife remained in England. In June or July, 1955, she realized she was pregnant, and on November 19 for the first time she informed her husband of her pregnancy. On December 2 she gave birth to a girl, telling her husband 10 days later. On January 11, 1956, Mr. Burgess told his wife he was stopping her monthly allowance, and proceeded to do so.

Ultimately Mrs. Burgess issued a summons in the High Court under s. 23 of the Matrimonial Causes Act, 1950, for maintenance on the ground that her husband had wil-

fully neglected to provide her with reasonable maintenance. The husband's answer was that he was under no duty to maintain her since she had deserted him or had committed adultery or that he reasonably believed her to have committed adultery. When the case was heard before Mr. Justice Collingwood the Court was invited to infer that the wife must have committed adultery with an unknown man by reason of the fact that the child had been born only 223 days after the last occasion on which Mr. and Mrs. Burgess had had intercourse and appeared to be a normal full-term child with no signs of prematurity.

Medical Evidence

Called to give evidence for the wife, Dr. C. G. Nairn said that the textbook average period of gestation of 280 days was reckoned from the onset of the last menstrual period. To work out the anticipated date of birth it was necessary to go back to the first day of the last menstrual period preceding a date of sexual intercourse and add 280 days to that, which would give only an approximately date of delivery at best. Therefore to the 224 days from April 22 to December 2 21 days could be added, making a total of 245 days of foetal life. Where, as in Mrs. Burgess's case, there was evidence of irregularity of periods a further 26 days should be added in the absence of definite evidence of a period, bringing the total up to 260 days. Even a 245-day foetus would not necessarily be obviously premature, and the general opinion was that an 8-months child could not with certainty be distinguished from one born at 9 months.

In his judgment rejecting Mr. Burgess's answer (*The Times*, March 28) Mr. Justice Collingwood said that since a finding of adultery would bastardize the child the court had to be satisfied beyond reasonable doubt. The evidence of Dr. Nairn could not be disregarded, and, accepting it as he did, it was clear that the child could have resulted from intercourse on April 22 or 23, 1955. There was no evidence that Mrs. Burgess had associated with other men at the material time, nor did the circumstances attending the birth have anything to do with Mr. Burgess's belief that she had committed adultery, which his Lordship held was unreasonable, nor had Mrs. Burgess intended to bring their cohabitation permanently to an end.

Accordingly the case was referred to the Registrar to decide the amount of maintenance to which Mrs. Burgess was entitled.

Universities and Colleges

UNIVERSITY OF OXFORD

In Congregation on May 1 the degree of B.M. was conferred on M. F. Burfoot.

UNIVERSITY OF CAMBRIDGE

Dr. D'A. Kok has been reappointed a University Lecturer in the Department of Medicine with tenure from October 1, 1958, for three years.

In Congregation on May 10 the following degrees were conferred:

M.B., B.Chir.—W. B. Peeling, E. A. French.
M.B.—*By proxy*: R. A. Aiken.

UNIVERSITY OF DUBLIN

SCHOOL OF PHYSIC, TRINITY COLLEGE

R. W. Childers has been approved at the examination for the degree of M.D.

UNIVERSITY OF LONDON

The following candidates of the Institute of Psychiatry have been approved as the examination indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN PSYCHOLOGICAL MEDICINE.—M. D. Eilenberg, L. Goldie, Q. A. F. R. Grant, W. I. N. Kessel (awarded a mark of distinction), N. B. McDiarmid.

UNIVERSITY OF LEEDS

Dr. M. D. Sumerling has been appointed Research Fellow in Radiodiagnosis for one year in the first instance from July 1, 1958.

UNIVERSITY OF SHEFFIELD

The following appointments are announced: Drs. P. F. Harris and M. Taylor, Lecturers in Anatomy; Dr. G. Haigh, Demonstrator in Anatomy.

UNIVERSITY OF BRISTOL

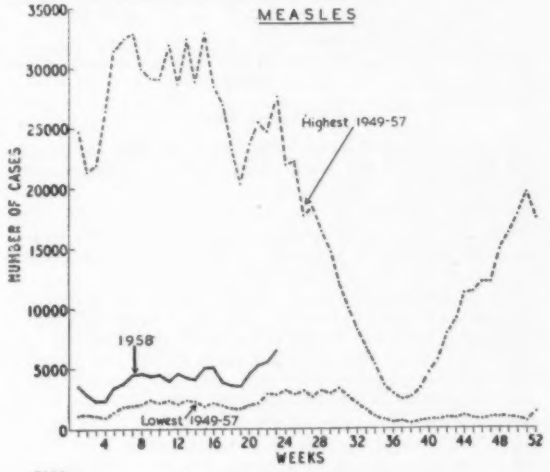
Drs. W. R. Lee, T. G. Ramsell, and P. J. Roylance have been appointed Demonstrators in Anatomy.

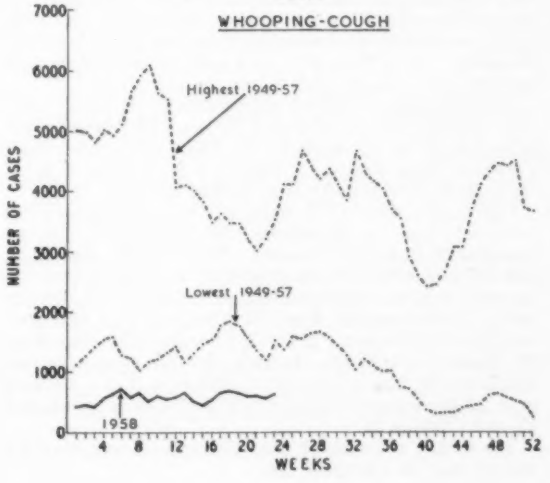
The following have resigned the appointments indicated in parentheses: Dr. Jean M. Sheach (Teacher in Radiodiagnosis); Dr. A. E. P. Twort (Medical Officer to Student Health Service); and Dr. A. J. Webb (Demonstrator in Anatomy).

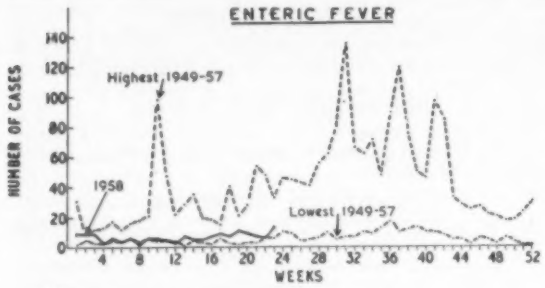
Vital Statistics

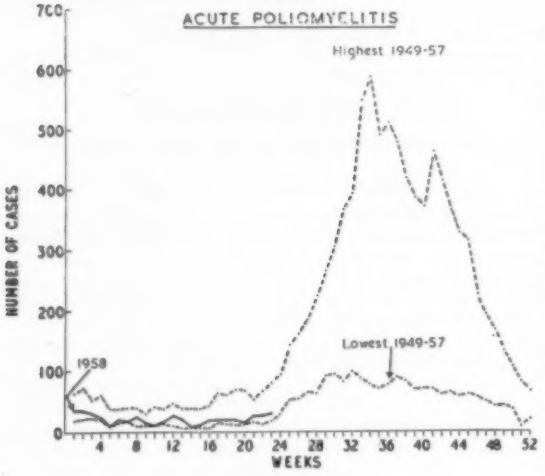
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1949–57 are shown thus - - - - - -, the figures for 1958 thus ———. Except for the curves showing notifications in 1958, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Week Ending June 7

Most infectious diseases were more frequent in England and Wales during the week ending June 7. The increases included 904 for measles, from 5,527 to 6,431, 102 for dysentery, from 781 to 883, 83 for whooping-cough, from 558 to 641, 46 for food-poisoning, from 138 to 184, and 26 for acute pneumonia, from 238 to 264; the only fall of any size was 40 for scarlet fever, from 653 to 613.

The largest increases in the incidence of measles were 238 in Middlesex, from 315 to 553 (Willesden M.B. 138), 155 in Lancashire, from 511 to 666 (Liverpool C.B. 185, Blackburn C.B. 118), 137 in Warwickshire, from 153 to 290 (Meriden R.D. 150, Birmingham C.B. 102), and 103 in Nottinghamshire, from 233 to 336 (Nottingham C.B. 172); the largest decreases were 80 in Sussex, from 182 to 102, 77 in Dorsetshire, from 116 to 39, and 59 in Lincolnshire, from 231 to 172. The largest fall in the number of notifications of scarlet fever was 20 in Lancashire, from 91 to 71. The largest increase in the incidence of whooping-cough was 29 in London, from 14 to 43. Two cases of diphtheria were notified, being 1 fewer than in the preceding week.

The notifications of acute poliomyelitis numbered 31 and were 6 fewer for paralytic and 10 more for non-paralytic cases than in the preceding week. The largest returns were Yorkshire West Riding 11 (Halifax C.B. 4, Leeds C.B. 3), Hampshire 5 (Winchester M.B. 2, Andover R.D. 2).

The largest centres of dysentery were Lancashire 164 (Liverpool C.B. 54, Manchester C.B. 27, Oldham C.B. 18, Rawtenstall M.B. 10), Yorkshire West Riding 149 (York C.B. 27, Leeds C.B. 17, Sheffield C.B. 17, Thorne R.D. 13, Barnsley C.B. 12, Bradford C.B. 12), London 85 (Wandsworth 21, Stepney 10), Essex 79 (Chigwell U.D. 60), Warwickshire 42 (Bedworth U.D. 22, Coventry C.B. 10), Surrey 40 (Banstead U.D. 37), Durham 33 (Gateshead C.B. 10), Middlesex 33, Gloucestershire 31 (Bristol C.B. 27), Staffordshire 29 (Newcastle-under-Lyme M.B. 13), Nottinghamshire 22, and Cheshire 21.

The largest outbreak of food-poisoning during the week was 26 cases in Liverpool C.B.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **May 31** (No. 22) and corresponding week 1957.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1958 Eng. & Wales	1958 Lond.	1958 Scot.	1958 N. Ire.	1958 Eire	1957 Eng. & Wales	1957 Lond.	1957 Scot.	1957 N. Ire.	1957 Eire
Diphtheria	3	1	1	0		1	0	3	0	1
Dysentery	781	69	204	12	3	740	47	273	10	7
Encephalitis, acute	6	2		0		4	1		0	
Enteric fever:										
Typhoid	5	0	0	0		6	0	0	0	
Paratyphoid	1	0	0	0		9	1	2(B)	0	1(B)
Food-poisoning	138	22	18	2		176	21	18	0	
Infective enteritis or diarrhoea under 2 years				7	18				18	20
Measles *	5,527	549	169	47	19	21,613	893	176	245	281
Meningococcal infection	19	4	12	0	1	26	3	14	1	
Ophthalmia neonatorum	17	1	12	0		29	2	9	0	
Pneumonia †	238	15	177	5		320	22	163	4	5
Poliomyelitis, acute:										
Paralytic	22	4	6	2	7	42	2	6	3	
Non-paralytic	5	2				25	0			
Puerperal fever §	200	29	8	3		9	1	15	1	1
Scarlet fever	653	38	87	24	16	691	58	76	22	21
Tuberculosis:										
Respiratory	530	54	135	9		646	74	278	24	
Non-respiratory	52	6	15	4		34	3	19	3	
Whooping-cough	558	14	66	23	34	1,807	69	206	6	41

DEATHS	1958 Eng. & Wales	1958 Lond.	1958 Scot.	1958 N. Ire.	1958 Eire	1957 Eng. & Wales	1957 Lond.	1957 Scot.	1957 N. Ire.	1957 Eire
Diphtheria	0	0	0	0	0	No comparable figures available.	0	0	0	0
Dysentery	0	0		0			0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0			0	0	0	
Infective enteritis or diarrhoea under 2 years	2	0	1	1	2		0	4	1	1
Influenza	14	0	0	0	0		0	0	0	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	0				0	0		
Pneumonia	320	27	17	14	10		15	16	10	11
Poliomyelitis, acute	1	1		1	0		0			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	69	5	3	0	5		5	11	1	4
Non-respiratory		0	0	0	2		0	1	0	0
Whooping-cough	0	0	0	0	0		0	0	0	0
Deaths 0–1 year	298	34	15	7			40	33	5	9
Deaths (excluding stillbirths)	8,791	716	600	125	166		710	568	120	157
LIVE BIRTHS	13,328	1155	1032	233	455		1250	986	267	347
STILLBIRTHS	271	24	23				22	22		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

B.M.A. Film Competition Awards.—On June 10 the President of the Association, Mr. WELDON WATTS, presented prizes to the winners of the 1957 B.M.A. film competition. The presentations were made at the Wellcome Foundation, 183, Euston Road, where afterwards the two winning films were shown to an invited audience. Dr. R. P. LISTON, chairman of the Association's Film Committee, introduced the President. Mr. WATTS said that since it began in 1946 the Film Committee had collected a library of over 400 films. The competition—the first the Association had held—had attracted 70 entries. He then presented the first prize in the non-commercial category to Mr. F. W. HOLDSWORTH, with the department of medical photography of the United Sheffield Hospitals, for his film, "Treatment of Paraplegia due to Fracture-dislocation of Dorso-lumbar Spine"; and the first prize in the commercial category to the Wellcome Laboratories of Tropical Medicine, with the Wellcome Film Unit, for their film "The Human Blood Fluke." Awards of merit, and a special commendation, were made to other competitors.

The Faculty of Radiologists.—Professor D. W. SMITHERS presided over the annual dinner of the Faculty of Radiologists on June 13. In proposing the health of the Faculty, Sir JAMES PATERSON ROSS said that when they wanted to find a new home during the war they came to the College of Surgeons in Lincoln's Inn Fields—the first Faculty to approach the College in this way. They now both shared the joint secretariat. Professor SMITHERS, in a witty speech of reply, confessed that as an honorary citizen of Texas he had narrowly missed being admitted as a deputy sheriff. He thanked Dr. WHATELY DAVIDSON for his successful three years of presidency of the Faculty. Dr. JOHN BROMLEY proposed the health of the guests and the response was made by LORD EVANS.

John Snow Centenary.—The centenary of the death of John Snow, the pioneer anaesthetist, who did much to dispel popular prejudice against general anaesthesia when in 1853 he administered chloroform to Queen Victoria for the birth of Prince Leopold, fell on June 16. The occasion was celebrated in London by the laying of wreaths on his grave at Brompton Cemetery by the president and members of the council of the Association of Anaesthetists of Great Britain and Ireland, the dean of the Faculty of Anaesthetists of the Royal College of Surgeons of England, and the presidents of the Sections of Anaesthetics and Epidemiology of the Royal Society of Medicine. Besides his classical work on ether and chloroform, John Snow is remembered for his demonstration of the water-borne spread of cholera in the London epidemics of his time.

Scholarships at Epsom.—In the issue of the *Journal* of October 5, 1957 (p. 814), attention was directed to the creation by the Medical Insurance Agency of a fund at Epsom College—to be associated with the name of Dr. Henry Robinson, hon. secretary of the Agency—to provide closed scholarships for the sons of registered general practitioners of either sex. So far as the College was concerned, the new principle of this offer was that awards were on a basis of academic merit solely, without any means test whatever. The first competition just held, by examination, attracted a large field of candidates. C. G. Van Essen was awarded a Henry Robinson scholarship of £250 per annum, and P. R. T. Newby (the son of a medical woman), the runner-up, a Leverhulme scholarship of the same amount, in each case as a boarder. A. D. Maclennan was awarded a Robinson scholarship of £75, to be held as a day-boy. Five open scholarships were awarded at the same time—though none of those successful was of medical parentage. Nine new foundationers have also been elected; in their case, as always, the basis was medical parentage and pecuniary distress. The funds necessary to defray their education come from the subscription income of the Royal Medical Foundation of Epsom College, for which the treasurer wishes to reiterate the Council's appeals to the profession. Further Robinson scholarships will be offered this time next year. Details about them may be obtained from the headmaster of the College.

Institute of Health, Singapore.—On May 14 Sir ROBERT SCOTT, H.M. Commissioner General for South-east Asia, presented the Institute of Health to Singapore as a gift from the United Kingdom. The cost of the Institute building—about £176,000—was met by a grant from the Colonial Welfare and Development Fund; the Government of Singapore gave land valued at £70,000, and Unicef equipment worth about £7,000. The Institute houses the department of social medicine and public health of the University of Malaya, city council maternal and child welfare clinics, and various Government clinics, such as for industrial health, mass radiography, B.C.G. vaccination, and dental and ophthalmic services. Teaching at the Institute includes courses for the D.P.H., courses in social and preventive medicine for medical students, and training for public health nurses and for health and antimalaria inspectors.

Minimum Requirements for Polio Vaccines.—Early this month an expert study group met at W.H.O. headquarters in Geneva to formulate internationally acceptable minimum requirements for the manufacture and testing of poliomyelitis vaccine. Many countries already have minimum requirements of their own, based in the main on those of the U.S.A. It would help, it is considered, to have international minimum requirements applicable to all the vaccines at present being made. This meeting was the first stage in establishing such requirements. Once the requirements are finally agreed upon, a useful step will have been taken to ensure that all poliomyelitis vaccines, regardless of the country of their origin, will have a high standard of potency and safety.

Chair of Midwifery, Durham.—Dr. J. K. RUSSELL has been appointed to the chair of midwifery and gynaecology at Durham University, where he has been senior lecturer in the subject. He succeeds Professor H. EVERS. Dr. Russell graduated from Aberdeen in 1942, proceeding M.D. in 1954. He was admitted M.R.C.O.G. in 1949 and was elected F.R.C.O.G. this year. Dr. Russell has carried out research on infertility and the causes of perinatal mortality.

Chair of Dental Surgery, Edinburgh.—Professor J. BOYES, F.R.C.S.Ed., Nuffield professor of oral medicine at Durham University and sub-dean of the Sutherland Dental School, has been appointed to the chair of dental surgery at Edinburgh. He will succeed Professor A. C. W. HUTCHINSON in October.

Cambridge University.—Dr. H. R. VICKERS has been appointed to a university lectureship in diseases of the skin. Sir RUDOLPH PETERS, F.R.S., has been elected an honorary fellow of Trinity College.

Royal College of Physicians of Ireland.—At a meeting of the College on June 6, the following members were admitted to the fellowship: K. M. Hickey, R. J. Kernohan, P. Logan, J. P. A. Ryan, D. S. Wilson, and (*in absentia*) M. Bhattacharyya. The following were admitted to the licence and membership: M. P. Awon, E. Casement, D. E. Donovan, V. T. Greene, and C. Lucey.

"Family Doctor."—The June issue includes an article by Professor R. S. Illingworth on children in hospital and an account of the 60 years' work of the R.A.M.C. by Major-General A. Sachs. With the issue is included a 16-page booklet on milk.

Chiropodists.—The Board of Registration of Medical Auxiliaries has issued a new edition (1957–8) of its *Register of Chiropodists*. Copies are supplied free to doctors and employing authorities, on application to the registrar of the Board, B.M.A. House, Tavistock Square, London, W.C.1.

North Western Thoracic Society.—The North Western Tuberculosis Society adopted a new constitution and altered its name to become the North Western Thoracic Society at its annual meeting on June 5.

John Scott Award.—Dr. A. J. P. MARTIN, F.R.S., formerly of the National Institute for Medical Research, Mill Hill, is one of five recipients of 1958 John Scott awards for inventions benefiting mankind. The award (a copper medal, scroll, and $1,000) is for his work on vapour-phase chromatography.

Oliver Bird Trust.—The trustees have awarded the 1957 Oliver Bird prize to DR. GREGORY PINCUS. The prize is for a paper on oral contraception and for the contributions made under his direction to the study of fertility control at the Worcester Foundation for Experimental Biology, Massachusetts.

Sir Walter Mercer, P.R.C.S.Ed., will receive the honorary degree of Master of Orthopaedic Surgery at the midsummer congregation of Liverpool University on July 4.

Dr. C. S. Hallpike, F.R.S., director of the Medical Research Council's otological research unit, was presented with the Bárány jubilee gold medal of the Medical Faculty of Uppsala University at a recent graduation ceremony there. Dr. Hallpike's work was described by Professor C. O. NYLÉN, professor of otology at Uppsala.

Dr. D. W. Abse, who graduated in medicine from Cardiff in 1938, has been appointed professor of psychiatry in the School of Medicine at North Carolina University.

COMING EVENTS

Macewen Memorial Lecture.—Professor CHARLES B. HUGGINS will lecture at Glasgow University on June 26 at 3 p.m. His subject will be "The Frontiers in Mammary Cancer."

Cambridge Graduates' Medical Club.—The annual general meeting and dinner will be held at Gonville and Caius College on July 4 at 7.15 for 7.45 p.m. Any member of the club who has not received notice of the dinner should write at once to Dr. T. B. ANDERSON, 1, Huntingdon Road, Cambridge.

Eighth International Congress of Catholic Doctors.—To be held in Brussels, July 27 to August 2. Details from the congress secretary, 5, Rue Guimard, Brussels.

Sir Vivian Fuchs will lecture on his journey to the South Pole, in aid of the National Varicose Foundation, on September 28 at 7.30 p.m. at the London Coliseum. Applications (marked "doctor" for priority allocation) for tickets, priced 5s., 7s. 6d., 10s. 6d., 15s., one guinea, and two guineas, should be sent to the treasurer, National Varicose Foundation, York Road, London, S.W.11.

NEW ISSUES

SPECIALIST JOURNALS AND ABSTRACTS

The journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

British Journal of Pharmacology and Chemotherapy.—Issued quarterly (£4 4s. annually). The new issue, Vol. 13, No. 2, includes :

CHRONIC TOXICITY OF DEXTRAN SULPHATE IN RABBITS. H. C. Hint and A. W. Richter.
VASOACTIVE SUBSTANCES IN THE NASAL MUCOSA. C. C. Toh and A. Mohiuddin.
A QUANTITATIVE METHOD FOR THE ASSAY OF INHIBITORS OF ACID GASTRIC SECRETION IN THE RAT. M. N. Ghosh.
STUDIES OF THE ACTION OF HYPOGLYCIN-A. A HYPOGLYCAEMIC SUBSTANCE. P. C. Feng and S. J. Patrick.
A COMPARISON OF SOME ACTIVITIES OF ARGININE VASOPRESSIN AND LYSINE VASOPRESSIN ON KIDNEY FUNCTION IN CONSCIOUS DOGS. M. N. Ali.
EFFECTS OF RATE OF STIMULATION AND OF FATIGUE ON THE RESPONSE TO NEUROMUSCULAR BLOCKING AGENTS. L. Wialicki.
METABOLIC FACTORS AND VENTRICULAR FIBRILLATION. P. J. Goodford.
COMPARISON OF THE EFFECTS OF ESERINE AND NEOSTIGMINE ON THE LEECH MUSCLE PREPARATION. B. K. Bhattacharya and W. Feldberg.
PERFUSION OF CEREBRAL VENTRICLES: EFFECTS OF DRUGS ON OUTFLOW FROM THE CISTERNA AND THE AQUEDUCT. B. K. Bhattacharya and W. Feldberg.
PERFUSION OF CEREBRAL VENTRICLES: ASSAY OF PHARMACOLOGICALLY ACTIVE SUBSTANCES IN THE EFFLUENT FROM CISTERNA AND AQUEDUCT. B. K. Bhattacharya and W. Feldberg.
ROLE OF QUININE IN HAEMOLYSIS. R. S. Grewal.
THE PRESSOR EFFECT OF PEPTONE IN THE RAT. W. T. Beraldo.
A COMPARISON OF SOME ATROPINE-LIKE DRUGS IN MAN, WITH PARTICULAR REFERENCE TO THEIR END-ORGAN SPECIFICITY. A. Herxheimer.
THE EFFECT OF ANTICHOLINESTERASES ON THE PAROTID GLAND AFTER PARASYMPATHETIC DECENTRALIZATION OR DENERVATION. N. Emmelin and B. C. R. Strömblad.
A METHOD FOR RECORDING THE EFFECTS OF ANTHELMINTICS ON THE MOVEMENTS OF ASCARIS LUMBRICOIDES. L. G. Goodwin.
THE TOXICITY OF 2-HYDROXYIMINOMETHYL-N-METHYL-PYRIDINIUM METHANESULPHONATE (P2S). D. R. Davies and G. L. Willey.
QUANTITATIVE ASSAYS OF OXYTOCIC DRUGS ON THE HUMAN POSTPARTUM UTERUS. P. R. Myerscough and H. O. Schild.

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature in the world. Annual subscription £4 4s.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, June 23

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. J. F. Goodwin: Pulmonary Hypertension.

Tuesday, June 24

BIOCHEMICAL SOCIETY.—At Department of Biochemistry, Tennis Court Road, Cambridge, 11 a.m., 374th meeting.
HEATHERWOOD ORTHOPAEDIC HOSPITAL.—8.30 p.m., Mr. P. S. London: Crushed Chests.
INSTITUTE OF CHILD HEALTH.—5 p.m., Professor J. H. P. Jonxis (State University, Groningen): Diseases Due to Abnormal Haemoglobins.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Less Common Mycotic Infections of the Skin.

Wednesday, June 25

BIOCHEMICAL SOCIETY.—At Department of Biochemistry, Tennis Court Road, Cambridge, 374th meeting continued.
DENTAL AND MEDICAL SOCIETY FOR THE STUDY OF HYPNOSIS: NORTH-WESTERN BRANCH.—At Manchester University (Main Building, Room 7), 8 p.m. Mr. E. E. Wookey and Dr. H. P. Tarnesby: Uses of Hypnosis in Medicine and Dentistry.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. D. O'Neill: Emotional Aspects of Skin Diseases (1).
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. R. W. Riddell: Anti-bacterial Agents in the Treatment of Tuberculosis.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. R. M. Fry: Some Reflections on Diagnostic Bacteriology.
ROYAL SOCIETY OF HEALTH.—At Town Hall, Chesterfield, 10 a.m., discussion: Food Hygiene Regulations and Food Poisoning. Speakers, Dr. E. H. Gillespie, Dr. A. I. Ross, and Mr. A. Wade.

Thursday, June 26

GLASGOW UNIVERSITY.—At Lecture Theatre, Chemistry Buildings, 3 p.m., Macewen Memorial Lecture by Professor Charles B. Huggins (Chicago): The Frontiers in Mammary Cancer.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. I. A. Magnus: Nickel, Chromium, and Eosin Epidermal Sensitization.
LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., special university lecture in medicine by Dr. George T. Pack (New York): Problem of the Pigmented Mole and Malignant Melanoma.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. James Sharp: Differential Diagnosis and Management of Spondylitis.

Friday, June 27

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. O. L. S. Scott: clinical demonstration.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. G. Scadding: clinical demonstration.
INSTITUTE OF NEUROLOGY.—5 p.m., Sir Macfarlane Burnet (Melbourne): Encephalitis in New Guinea.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—10 a.m., Mr. A. W. Kay: Pyloric Antrum and Peptic Ulceration. 2 p.m., Dr. Henry Harkins (Seattle): Surgery as Practised in Europe and the United States—A Comparison.
SOCIETY FOR ENDOCRINOLOGY.—At Royal Society of Tropical Medicine and Hygiene, 5.30 p.m. Annual Lecture by Professor O. Mühlbock (Amsterdam): The Hormonal Genesis of Mammary Cancer.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Last.—On June 7, 1958, at University College Hospital, London, W.C., to Pauline (formerly Weeks) and Rex Last, of 2, Newnton Close, London, N., a daughter—Sarah Ann.

DEATHS

Eccleston.—On May 22, 1958, at his home, 177, Mauldeth Road, Withington, Manchester, Charles Eccleston, M.B., Ch.B.
Evans.—On May 29, 1958, in hospital, Douglas Gordon Evans, M.B., B.S., Major, R.A.M.C. (retired), of 4, Palace Road, East Molesey, Surrey, aged 72.
Head.—On May 29, 1958, at his home, Southdown House, Storrington, Sussex, Alfred Joseph Head, M.B., B.Ch., aged 63.
Herman.—On May 26, 1958, Walter Sebastian Herman, M.R.C.S., L.R.C.P., L.D.S., of 18, Harley Court, London, N.
Heylen.—On May 29, 1958, Albert Heylen, M.D., of 161, Philip Lane, Tottenham, London, N.
Jones.—On May 24, 1958, at 229, Drumchapel Road, Glasgow, David Harris Jones, M.B., Ch.B.
Knox.—On May 27, 1958, at his home, 9, Grosvenor Place, Bath, Somerset, Robert George Knox, M.R.C.S., L.R.C.P.
McDougall.—On May 27, 1958, at Brachead, Newmills, Fife, Donald McDougall, M.B., Ch.B., late of Isle of Arran.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Relaxant Drugs in Infertility

Q.—*Are relaxant drugs of use in cases of infertility due to spasm of the Fallopian tubes?*

A.—Drugs such as preparations of curare and synthetic relaxants now used in conjunction with anaesthesia act only on voluntary muscle. They probably have no effect on the muscle of the uterus and tubes, although a slight stimulatory action is described by some workers. These drugs are therefore not indicated in the circumstances described. Antispasmodics such as belladonna, atropine, benzyl benzoate, amyl and octyl nitrite, papaverine, nitroglycerin, hydrogenated alkaloids of ergot, and various proprietary preparations are, however, sometimes used in the hope of relaxing spasm of the utero-tubal junctions which might be lowering fertility. One of the earliest workers to suggest this line of treatment was S. R. Meaker,[1] but many have written of it since. If these drugs are used they are administered immediately before and after coitus, especially coitus taking place about the time of ovulation. Unfortunately, with the possible exception of nitrites, there is no evidence to show that any of the substances mentioned above can relax spasm of the tubes and uterus. Indeed, there is reason to believe that some of them increase muscle activity at these sites. Moreover, it is established statistically that those women shown to have utero-tubal spasm at the time of insufflation or salpingography subsequently conceive just as frequently without treatment as when they are given alleged antispasmodics.

REFERENCE

1 Meaker, S. R., *J. Amer. med. Ass.*, 1924, **82**, 2098.

Age of a Bruise

Q.—*Is it possible to say within a space of hours what is the age of a bruise?*

A.—It is extremely difficult to date a bruise in a living person to within a few hours. If a bruise shows gross changes in colour then it is usually about three to four days old. In the first 24 to 48 hours it would be most unwise to offer an opinion other than "recent" or "fairly recent." Swelling may give some hint as to how recent. At necropsy, however, histological examination will show leucocytic infiltration after a few hours, and Moritz[1] quotes: "Higgins and Palmer[2] observed that the polymorphonuclear leucocytes in a haematoma begin to disintegrate after three to five hours, that they are for the most part fragmented within 21 hours and that by 30 hours the basophilic nuclear fragments have either undergone autolysis or have been engulfed by the phagocytic monocytes."

REFERENCES

1 Moritz, A., *Pathology of Trauma*, 1942, 1st ed., Chapter I, pp. 23 and 24. Lea and Febiger, Philadelphia.
2 Higgins, G. M., and Palmer, B. M., *Arch. Path.*, 1929, **7**, 63.

Toxicity of "Albamycin"

Q.—*Does albamycin (calcium salt of novobiocin) have a toxic effect on the liver?*

A.—Albamycin appears to exert a toxic action on the liver. R. A. Bridges, H. Berendes, and R. A. Good[1] describe the effect of giving novobiocin and cortisone to a boy with general sepsis who was thought to have rheumatic fever. He died, and at necropsy was found to have diffuse hepatic necrosis. It was considered most likely due to the novobiocin. A report from the Upjohn Company states that dogs given 300 mg./kg. daily developed severe degenerative changes in the liver and kidneys. The *Journal of the American Medical Association*[2] says that the drug causes a yellow pigment to be formed which interferes with the determination of serum bilirubin. This is stated to be a metabolite of the drug rather than a bile pigment. Thus all authorities are not agreed about the toxic action on the liver.

REFERENCES

1 Bridges, R. A., Berendes, H., and Good, R. A., *J. Pediat.*, 1957, **50**, 579.
2 *J. Amer. med. Ass.*, 1957, **163**, 646.

Placental Extracts in Dermatology

Q.—*What is the rationale for the use of placental extracts for treatment of varicose ulcers and other skin conditions?*

A.—The use of placental extracts for the treatment of leg ulcers and other conditions arose from Filatov's work in Russia, from 1933 onward, on corneal grafting. He believed that the graft could not be considered solely as a transparent window but also as a stimulus to regeneration of the cornea. Various tissue extracts were believed to be biological stimulants, and since then extracts of aorta, placenta, muscle, and brain have been used by European workers (in particular the French) both for local application and for intramuscular injection. Implants of these tissues have also been employed. In this country Troensegaard-Hansen[1] claimed good results in the treatment of chronic leg ulcers by the application of boiled amnion, a method of treatment reminiscent of that of Critchett,[2] who in 1849 advised that such ulcers should be covered by the lining membrane of eggshells. Other workers who have used Troensegaard-Hansen's method have not obtained the same excellent results. Troensegaard-Hansen[3] has used implants of amnion in the treatment of intermittent claudication, but Moore[4] and others have been unable to achieve the same success. The whole question of the effects, if any, of tissue extracts on the healing of ulcers or the relief of intermittent claudication is still a matter for debate.

REFERENCES

1 Troensegaard-Hansen, E., *Lancet*, 1950, **1**, 859.
2 Critchett, G., *Lectures on the Causes and Treatment of Ulcers of the Lower Extremity*, 1849. London.
3 Troensegaard-Hansen, E., *Brit. med. J.*, 1956, **2**, 262.
4 Moore, H. D., *ibid.*, 1957, **2**, 1350.

What Foods?

Q.—*What foods contain (1) essential fatty acids; (2) vitamin B_6?*

A.—(1) Vegetable oils, such as maize, cottonseed, and pea-nut, are rich sources of "essential" fatty acids, which are also widely distributed in cereals, green vegetables, nuts, and some animal fats, such as lard.

(2) According to values quoted by Bicknell and Prescott,[1] vitamin B_6 is present in wheat germ (6–17.5 μg. per g.), whole-meal flour (4.2), white flour (1.8), dried yeast (3–4), potatoes (2.2–3.2), "marmite" (4.0), molasses (2.7), dried peas (3), dried beans (5.5), roasted peanuts (3.0), bananas (3.2), mackerel (2.1–2.7), salmon (4.5), and sardines (1.6–2.8). Numerous other foods contain smaller amounts.

REFERENCE

1 Bicknell, F., and Prescott, F., *The Vitamins in Medicine*, 1953. Heinemann, London.

Anaemia and Puerperal Psychosis

Q.—*Is there any known connexion between an iron deficiency or macrocytic anaemia and puerperal psychoses?*

A.—Puerperal psychoses are not any distinct clinical group, but include, for instance, schizophrenia, manic depressive illness, or toxic confusional states. There is no suggestion that anaemias of any kind are particularly connected with either of the first two, but they may easily be connected with the third. However, the anaemia of pregnancy, which is fairly common, is usually corrected before the confinement, and if anaemia is discovered only after that its causation is usually obscure, as it may easily be due to

blood loss in childbirth. Pregnancy aggravates idiopathic hypochromic anaemia, so this form of anaemia might possibly be connected with puerperal confusional states. However, it is itself usually no more than a part of a generalized syndrome, including nutritional deficiencies, bad living conditions, etc., all of which could separately have a causal connexion with puerperal mental illness.

Finally, as to the macrocytic anaemias, pernicious anaemia is very rare before the fourth decade, and so is not often combined with the puerperium. I believe that there is a macrocytic anaemia which occurs in pregnancy for unknown causes, but it is rare. There are still other anaemias, such as sprue, which have to be taken into account which are themselves of obscure causation and seem to be related to such a complex syndrome as puerperal psychosis only in the most speculative way.

Physiotherapy for Parkinson's Disease

Q.—*What type of physiotherapy would improve the gait in a case of Parkinson's disease?*

A.—A succinct answer to this question would be "an intelligent physiotherapist." Treatment would consist of remedial exercises, but these would have to be applied with great patience and understanding. Overcorrection of faults of gait and posture must be taught and its maintenance emphasized. A mirror may prove helpful to some patients in understanding this treatment. Music is found helpful by some. There is little place for electrical treatments, hydrotherapy, or massage.

Cough Suppressants

Q.—*Are pholcodine, ethane disulphone, and dihydrocodeinone superior to codeine phosphate in relieving unproductive cough?*

A.—It is widely believed that codeine is an effective cough suppressant. In both experimental studies and controlled clinical trials, however, it has been shown to be relatively ineffective when compared with morphine or its analogues diamorphine and methadone. Dihydrocodeinone is also a morphine derivative, and, although it is an effective cough suppressant, it shares with morphine and diamorphine the grave drawback that it is a drug to which addiction and tolerance may occur. Pholcodine in the form of a linctus has been shown in a recent clinical trial to be as effective a cough suppressant as diamorphine, and it is not a drug of addiction nor does it produce constipation. Ethane disulphone has not been investigated so fully but is reported to be a good cough suppressant which does not give rise to addiction, and in the recommended therapeutic doses is said to be safe for prolonged administration even to children. Methadone linctus (*N.F.*) is a well-tried and effective preparation for the relief of cough. It should, however, not be used for long periods, as methadone is a drug of addiction.

Prednisone in Asthma

Q.—*Should prednisone be given early in a severe attack of asthma in a patient who has attacks about once a month which do not respond to adrenaline and aminophylline?*

A.—It is justifiable to give prednisone to any asthmatic in status asthmaticus who has failed to respond to adequate subcutaneous adrenaline and intravenous aminophylline. The dose of cortisone used in the M.R.C. trials[1] was 300 mg. on the first day, 200 mg. on the second and third days, and 100 mg. on the next four days in divided doses. The local physician then adjusted the dose to suit the needs of individual patients. Davies and Williams[2] used a very similar dosage for status asthmaticus, but recommended for intractable asthma a trial of 100 mg. a day for four days and 75 mg. a day for three days. In the main, treatment was continued for seven to 14 days, until the chest had been clear for a few days. 5 mg. of prednisone is roughly equivalent to 25 mg. of cortisone. Cortisone, and especially prednisone, will exacerbate peptic ulceration and is best not given in such cases, except as a "measured risk"; mental disturbances may occur in those who have had previous severe nervous breakdowns; cortisone and prednisone will exacerbate diabetes and the former especially tends to cause hypertension and fluid retention.

The frequency and severity of the attacks in this patient suggest a need for a full investigation of the underlying causes. Very frequent intermittent hormonal therapy would not appear to be a reasonable line of treatment. Long-term hormonal therapy (cortisone 50 mg. daily (75–25 mg.) or prednisone 10 mg. daily (5–15 mg.)) is still under review, and while most helped in the initial months, in a proportion it then becomes ineffective. In long-term therapy constant care is necessary to avoid dangerous side-effects, even though uncommon, on this dosage. A leading article on this subject appeared in the *Journal* of May 17 (p. 1166).

REFERENCES

[1] *Lancet*, 1956, **2**, 798.
[2] Davies, B. M., and Williams, D. A., *Brit. med. J.*, 1955, **2**, 293.

Pustular Psoriasis

Q.—*What is the treatment for pustular psoriasis of the soles of the feet?*

A.—The treatment is extremely difficult and the eruption in this situation is much more difficult to remove than ordinary psoriasis in other parts of the body. In general the same treatments are effective, and occlusive dressings of tar such as "coltapast" may be particularly valuable. The recent review by Everall[1] indicates that the treatment of focal sepsis, often considered very important in these cases, probably does not influence the course of the eruption.

REFERENCE

[1] Everall, J. D., *Brit. J. Derm.*, 1957, **69**, 269.

Sulphonamides and Hair

Q.—*Is it true that the presence in the body of sulphonamides has an adverse action on the tinting, dyeing, or "perming" of hair?*

A.—It is difficult to believe that it should be so. The hair is composed of keratin, a non-living substance, and the hair shaft has no chemical communication with the blood circulation or with the living tissues. The presence of sulphonamides in the body, therefore, should have no effect on the hair.

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